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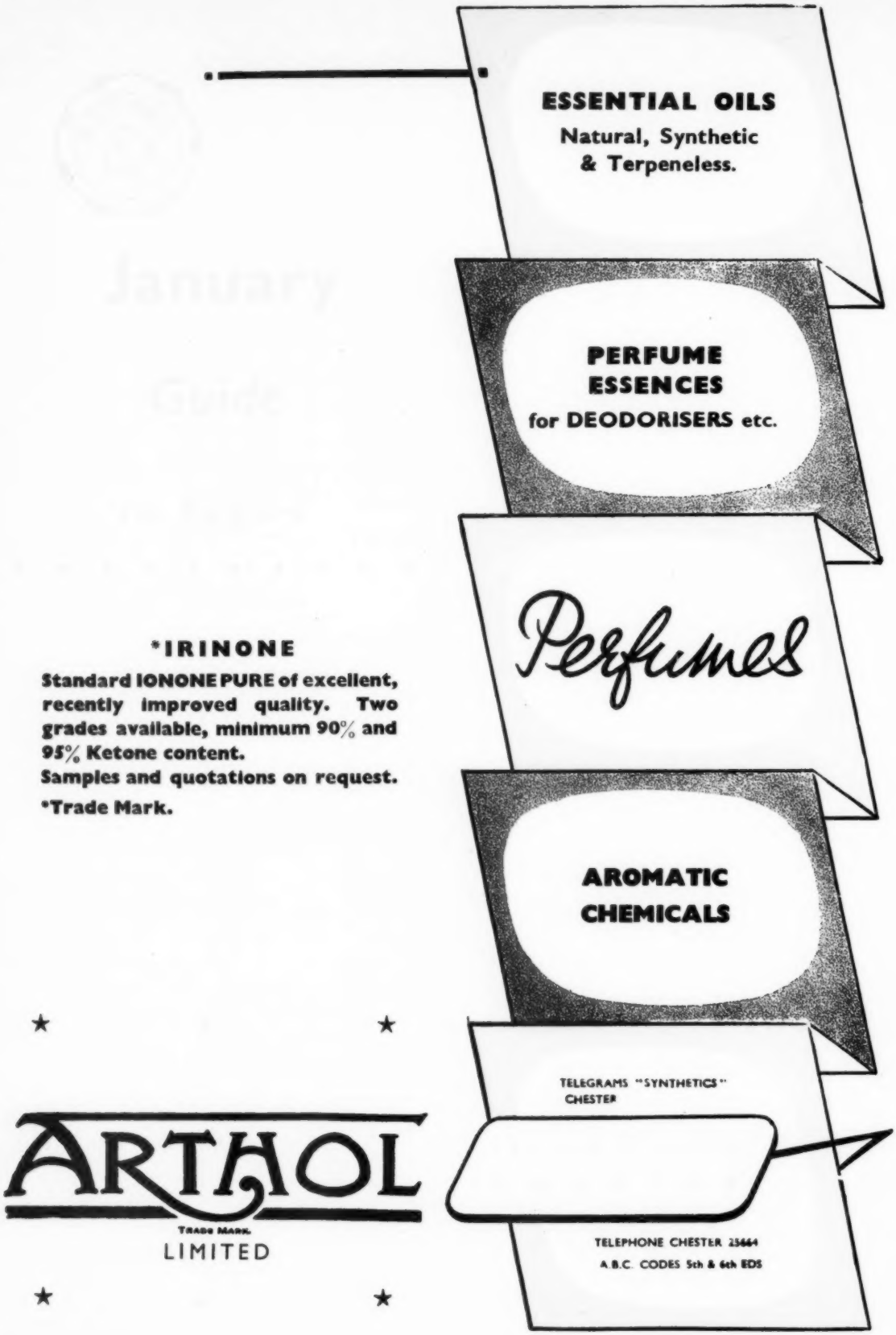

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TOPICS AND COMMENTS

Makers of medicine

UNDER this short, alliterative title, the Association of British Pharmaceutical Industry has put out a leaflet summarising in brief and meaningful phrases the achievements of its 170 member companies. The following extract typifies the forthright style of the leaflet:

"The British pharmaceutical industry—
provides employment for over 50,000 people
operates 450 establishments
and in a year
contributes £150 million to the gross national output
exports £40 million worth of goods
provides the drugs for over 200 million prescriptions
and spends £5 million on research."

It is pointed out that without the more recent products of the industry it would be impossible to fill four out of the five prescriptions which the family doctor writes today. The drugs just would not exist.

The daily, almost hourly, contact of the industry with the people is emphasised in homely phrases. "Call at any house, in any street in Britain, and speak to the man who lives there. You would find that the products of Britain's pharmaceutical industry have been close to him at the moment of his birth . . . for his Army inoculations . . . for his visits to the dentist . . . when he had to take his dog to the 'vet' . . . when his daughter had her polio injection."

Like all good propaganda the leaflet is brief, direct and truthful. It has been produced for A.B.P.I. firms to distribute to members of the public who visit them and who are otherwise interested. No one who reads it can continue to think of the industry as a vague, amorphous group of factories turning out the pills and potions of the old-fashioned chemist. It is up to the industry to see that it gets the widest possible circulation.

Value for money

ARE too many people making too many profits out of selling drugs to the American public? That is the basic question being asked by the U.S. Senate anti-trust and monopoly sub-committee which has been investigating the American ethical drug industry and which will, after the year-end recess, continue its investigations. Modern medicine, comments the *Times* correspondent, has given the average American another 10 years to live but for many those 10 years have become cripplingly expensive. Sales of drugs on prescription have risen from 500 million dollars (£171,571,000) in 1945 to 2,200 million dollars (£785,714,000) in 1958. The average price of a doctor's prescription has risen by more than a third in 10 years and now costs 3 dollars, about a guinea. Even on a per capita comparison, Britain's drug bill is almost paltry compared with America's. Since 1949 the average cost per prescription has increased from 3s. 1d. to 6s. and the total cost of prescriptions to about £63 million a year. With a population of under four times the size of the U.K., the United States is spending over 12 times as much on prescription drugs. It would certainly appear that the American public is paying a very high price for the privilege of having the biggest pharmaceutical industry in the world. The Federal Trade Commission has fastened on the fact that the industry's rate of profit in 1957 was 22% of its net value, the highest in any major manufacturing industry and twice the general average.

Looking at the above statistics in terms of research it appears that the British drug industry is actually making a better effort proportionately than the American. Our research expenditure is just over £5 million p.a., a little below one-eighth of the American, which is £43 million p.a. Expressed as a percentage of the value of prescription sales in each country, the British figure is 8% and the American less than 6%. Perhaps it is not too much to say that the British pharmaceutical industry gives better value for money than any comparable industry.

Cephalosporin—a successor to penicillin?

THE most promising chemical project of the National Research Development Corporation appears to be the new antibiotic cephalosporin C. It is closely related to penicillin but is different in chemical structure and biological properties. Its most significant difference is its resistance to destruction by penicillinase. The exact chemical structure of cephalosporin C is unknown but attempts are being made to elucidate it. Mrs. Dorothy Hodgkin, at Oxford University, is using X-ray crystallography to help determine the structure and is being helped financially by the Corporation.

Cephalosporin C is mentioned briefly in the Corporation's 1958-59 report, just issued. Patent applications for the drug have been filed in several countries and "a large British antibiotic-producing firm" has been associated with the project to help work out production methods. Since the "large firm" referred to could only be one of three, one wonders why it was not named. In fact it is Glaxo Laboratories Ltd. Could cephalosporin C be the antibiotic that Beecham are working on in conjunction with their work on the penicillin nucleus?

Three more chemical projects

APART from cephalosporin, there are two new N.R.D.C. development projects of chemical interest. An automatic apparatus for the chemical treatment and scanning of chromatograms, invented by Dr. I. E. Bush of the Radcliffe Infirmary, Oxford, is being sponsored. His prototype instrument is nearing completion.

Work on compounds with an adrenaline or anti-adrenaline action is being aided. The work is being done in the Royal Free Hospital School of Medicine under Prof. Eleanor Zaimis and Dr. A. Lawson.

Among older projects there is the scheme for producing acetylene by partial combustion of methane. The development of this process, which was started at Imperial College, London, has been transferred to a small laboratory set up by the Corporation at the Mogden Drainage Works of the West Middlesex County Council, where continuous supplies of methane are available from sewage processes. A burner system has been developed which gives higher concentrations of acetylene than those obtained in current industrial practice. The process could provide a rich new source of organic chemicals and its commercial exploitation is being explored with a number of manufacturers.

Nearly 700 inventions were communicated to the Corporation during 1958-59 and 187 patent rights were assigned to them, both figures being somewhat higher than in the previous year.

At the end of the year under review they held the rights in 2,794 United Kingdom and foreign patents or patent applications, of which 1,038 were being actively exploited; and 395 licence agreements with manufacturers were in force, as compared with 357 in the previous year.

Chemical engineers' pay

How much do chemical engineers earn? As can be seen from vacancies advertised in newspapers and in the technical press, salaries vary widely according to the size of the firm, the nature of the industry and the kind of work (design, development, construction or operation) for which the vacancy exists. However, a booklet published by the Institution of Chemical Engineers takes a courageous stab at setting out an approximate scale of salaries, noting, for instance, that five-year student apprentices are paid about £5 10s. to £6 10s. a week at the age of 18, rising to £9 or £10 a week at 23. In a number of large companies, starting salaries range from about £600 p.a. for "pass" graduates in chemical engineering to about £800 or £900 for an honours graduate with a post-graduate qualification such as Ph.D.

The competent chemical engineer may well double his salary by the time he has reached his early thirties, but after that there is a great variation in the maximum salary paid. This is not surprising, since, as the booklet points out, chemical engineers are to be found in the higher administration and in the direction of research and development in many companies.

The Institution's new booklet, entitled "Education and Training in Chemical Engineering," brings together in one tidy and useful little publication various leaflets and other material released by the Institution from time to time. It includes a brief comment on the subject of women chemical engineers, vacancies for whom are limited at present as there is a reluctance in industry to employ women in plant management. It is prophesied that opportunities for women in chemical engineering will increase and that, as employers become more used to the idea of calling on both sexes to obtain the qualified people they need, women will gradually attain equal status with men, as in other professions.

Neglect of education

DURING the next 10 years Britain's university population may rise to 150,000. That will be more than a 50% increase on today's figures and some people may think this very creditable. Unfortunately even if we reach our 10 year target we shall still have fewer students in universities than France, West Germany and Italy have *today*. The dismal truth is that in a list of 27 countries we are fourth from the bottom in terms of the number of university students per million of population. Only three countries—Ireland, Turkey and Norway—have fewer students per million than Britain. Our figure is 1,815 per million, less than half that of 16 countries, including —apart from the obvious instances of Russia and the U.S.—Argentina, Poland, Bulgaria and Australia. Even if the U.K. figure is doubled by including students at technical colleges, we still have fewer students per million than 16 other countries.

Around startling and depressing facts like these the Principal of Manchester College of Science and Technology, Dr. B. V. Bowden, has constructed an indictment of Britain's attitude towards higher education. It appears in the *Universities Quarterly* and extracts have been printed in the *Guardian* newspaper.

In 1870 a gentleman called Mark Pattison complained that the universities could not find any more students worth educating—there were then fewer than 5,000 undergraduates in Britain. It seems that this view still prevails, for only 6% of our schoolchildren are deemed fit for a university education compared with 35% of American children. An American child is three times as likely to go to a university as an English child is to go into a sixth form. Of course our university authorities set higher entrance standards than the Americans. In some American universities 40 to 50% of students fail and leave after the first year. Even a fraction of this failure rate would horrify our universities. But the Americans still think that a year in a university is of value even to a man who cannot stay the pace. Their system may be relatively extravagant and inefficient,

but it is extremely effective and productive because of the sheer number of students who go to universities.

Dr. Bowden refuses to accept the superior view of some English educationalists that our university standards are so much higher that we need not worry about our deplorably small number of students. Perhaps only 100 American universities may be of the standard of ours—out of 1,840 universities and colleges. But the best are as good as ours and their élite get as good a training as ours. And in addition they try to give better opportunities to a much greater number of the population than we do. This must count in the long run. Dr. Bowden reports that in Manchester the quality of the students improves as their number increases.

An obvious comment on Dr. Bowden's strictures is that if we are so backward in providing university education, how is it that we are more prosperous than so many of the countries with better educational facilities. The answer surely is that we are still living on the accumulated fat of a century of industrial and technological dominance. The momentum provided by the great Victorians still carries us along. But what are we doing to regenerate this onward movement? We spend £37·3 million on university grants and £47·6 million on the egg subsidy. Eggs are more important than eggheads, apparently. We spend £557 million on the Health Service to treat disease and a miserable £3·1 million on the Medical Research Council to find out how to treat and prevent disease.

The absurdity of this scale of priorities needs no emphasis. Dr. Bowden has a vested interest in the matter, but he has every right to pillory the authorities for allowing us to fall so far behind, and the nation at large for its smug and complacent acceptance of the situation.

Dollars for deadly daisies

EAST AFRICA's marguerite-like flower, pyrethrum, is expected to earn 5,600,000 dollars in the 12 months ending June next. This is the value of the insecticidal liquid extract and powder obtained from pyrethrum flowers which the U.S. is expected to import during that period.

The forecast is made by the semi-official Pyrethrum Board of Kenya which acts on a co-operative basis for the European and African farmers who grow pyrethrum on the high plateaux of Kenya and the Belgian Congo. The pyrethrum flower crop in Kenya is expected to amount to 6,500 tons with an estimated export value of the flower, or of the insecticide extracted from it, of £2½ million, of which exports to the United States will account for about £2 million.

The crop estimate of 6,500 tons is an increase of 2,450 tons, or more than a third, over last year's actual crop. This year's larger crop, however, is less than planned at the beginning of the current period, adverse weather having restricted growth of the flowers. According to the present trend of its order book, the Board estimates that it could have sold overseas some 12% more than the estimated 1959-60 crop.

To meet steadily increasing overseas demand from insecticide manufacturers the Board foresees a production in the ensuing year, by European and African farmers, of 8,000 tons of pyrethrum flower with an export value, mainly in the form of pyrethrum extract, of over £3 million.

The Pyrethrum Board of Kenya has built its own extraction plant at Nakuru, in the heart of the pyrethrum growing area of Kenya. The factory came into commercial operation in March this year and is already being extended. Export in the form of baled flowers, which is bulky, is decreasing, with a corresponding increase in the export of the extract, much of which now goes to many parts of the world by air.

Patents in Russia

CAN inventions be patented in a State that has abolished private industry? British manufacturers wishing to increase their trade with the Soviet Union must often have asked this question. The answer, surprisingly, is "yes." Of course, there are several qualifications, and to find out just what chance a British firm has of protecting its inventions in Russia, Mr. Gordon Grant, Comptroller-General of Patents, and two colleagues recently visited Moscow to talk to their Russian counterparts. The Russian equivalent of the Patent Office proved to be the Committee on Inventions and Discoveries under the Council of Ministers of the U.S.S.R. The people who deal with the commercial aspects of patents are the All-Union Chamber of Commerce.

An inventor, Russian or foreign, has by Soviet law the option to seek either a patent, which gives him a monopoly in his invention which no one may then use without his permission, or an "authors certificate." In the latter case he assigns his invention to the State, which pays him according to the amount of use made of his invention and the resultant saving to the economy. Since the latter system involves the inventor in less expense and fits into an economic system in which all the means of production are controlled by the State, Soviet inventors invariably seek authors certificates rather than patents. Foreign owners of inventions, on the other hand, tend to seek patents.

The new Soviet law of April 1959, *so far as it concerns patents* does not differ in its essentials from the laws of the other countries of the world. There is, of course, in the absence of *Contractual* obligations, nothing to stop the copying of foreign inventions in the Soviet Union unless they are patented *there*. But the Soviet law, like those of other countries, provides the means whereby, if the necessary steps are taken, inventions can be protected. Before a patent is granted the invention must be described in a specification and a search is made through Soviet and foreign patents and technical literature to make

sure that the invention is new. It must also have actual or potential "industrial utility," *i.e.* it must be in a field which, in the opinion of the competent Soviet technical organisation, is one in which there is or is likely to be activity. This latter test finds no place in the U.K. system, which demands instead that the invention be not "obvious." If the invention passes these tests a patent is granted and, provided renewal fees are paid each year, the patent lasts for 15 years from the date of application. Subject to the powers reserved to the State to issue compulsory licences (on payment of remuneration to the patentee) "where an invention is of special importance to the State"—and there is something like this in the laws of most countries—it is an offence, during this period, to use the invention without the patentee's consent. The delegation was told that the patentee's monopoly embraces not only the right to prevent others from making goods incorporating the invention but also the right to prevent them from importing such goods.

If a Soviet factory wishes to use an invention the Soviet patent for which is owned by a foreigner, the latter is notified by the Chamber of Commerce. The actual contract is negotiated by the Soviet Ministry of Foreign Trade and one of the import-export corporations.

On the question whether or not a patent (or authors certificate) shall be granted, the Committee on Inventions and Discoveries has the final word. The Committee has its own appeals procedures which, the delegation were told, include a right for the inventor to appear and be heard. Disputes as to the *ownership* of inventions are heard by the ordinary courts. If infringement of a patent is suspected the Committee would, it seems, look into this. In addition the delegation was told, by the Ministry of Foreign Trade, that infringement actions can be brought before the ordinary courts. It seems reasonable to assume, however, that no such action has ever been brought.

The Soviet officials who received the delegation expressed themselves as anxious to avoid any misunderstanding. It was clear that they were interested in foreign patent practice and the delegation got the impression that, so far as the different economic systems permit, were tending to bring their law and practice into line with those followed elsewhere.

Little use has so far been made, by United Kingdom owners of inventions, of the Soviet patent system and there is therefore little practical experience. The language problem and the widely differing concepts of the rights to be enjoyed by the individual as against officials will no doubt lead to some problems. But it seems clear that, at the worst, the owners of worthwhile inventions who contemplate trading with Russians can only lose the fees they pay and, from the assurance given to the delegation, may well have a good deal to gain if they patent these inventions in the Soviet Union. In the light of this it seems only reasonable that the Soviet system should be given a fair trial.

Million pound fires

THE chemical industry can count itself fortunate that the nature of its processes does not require large open plan factories. Mass production industries, such as motor-car manufacturing, need enormous open areas to accommodate production lines and these factories are terribly vulnerable to fire damage because of the absence of fire breaks. Catastrophic fires like these are responsible for 1959 having been a record year for fire losses. At least £40 millions of damage were caused by fire last year, and in 1958 and 1959 there were five fires each causing damage of over £1 million. Fire experts fear that the day of the £10 million factory fire is approaching.

This is the sombre background to the National Fire Protection Conference, sponsored by the Fire Protection Association, which will be held in London on February 25 and 26. Full Government support is being given to the conference.

The Government will be represented by Mr. R. A. Butler, the Home Secretary, who is to address the conference, and Mr. Edward Heath, the Minister of Labour, who will be the principal guest at the conference dinner on February 25.

Translator's nightmare

THE young State of Israel is rapidly becoming the leading technical and industrial nation in the Middle East. Men and money have been poured into industries like drugs, chemicals, plastics and engineering. But in insisting, quite naturally, on using Hebrew as the official language, the authorities have set for themselves a formidable problem. Hebrew translators of scientific and technical literature have the impossible task of rendering modern works in an idiom which even twelfth-century scholars abandoned as obsolete and unfit for their purpose. Modern scientific terms can be and are borrowed freely from European languages, but the difficulty lies in the archaic structure of Hebrew. It is like trying to turn a chariot into a supercharged racing car. One amazing defect of Hebrew is that it has no vowels, only consonants. So the pronunciation and meaning of a written word can only be determined after the reader has guessed the approximate meaning of the whole phrase. It would appear that the only solution is the Latinisation of the Hebrew alphabet. The Chinese and the Japanese are also conscious of the handicap of their thousands of ideograms and want to replace them with the efficient 26 letters of the Roman alphabet. But even Communist dictators hesitate to make such a wholesale reform of the people's language, with all its tremendous emotional and political implications. India has evaded the issue for the time being by temporarily retaining as the official language that priceless gift of the British Raj—English. For better or worse English is the most widely used language of science and technology, and countries which are able to use it only harm themselves by trying to put the clock back by reviving their ancient languages.

The Continuous Culture of Micro-organisms and its Industrial Applications

By Charles G. T. Evans, M.SC.

Micro-organisms have enormous potentialities as producers of drugs and chemicals and a great deal of work is being done to make fermentation processes more efficient and more profitable. Here the author examines the present state of development of continuous culture processes and discusses their industrial potentialities for the production of antibiotics, enzymes, food supplements, lactic acid and other fermentation products.

DURING recent years, the phrase " continuous culture " has acquired among microbiologists following the work of Monod (1950) a specialised meaning signifying a particular technique; thus growing organisms by a continuous process need not necessarily imply a process of continuous culture in the new sense. In order to make this distinction, it has been suggested by Herbert and Powell (private communication) that the terms " homogeneous continuous culture " and " heterogeneous continuous culture " should be used for the newer and the older meanings respectively. This is done throughout this article. Homogeneous continuous culture implies that the organisms are caused to grow indefinitely at an exponential rate which can be approximately equivalent to the logarithmic growth phase of conventional batch culture. In this phase the organisms are metabolically most active and it is often referred to as the phase of physiological youth.

The rate at which organisms will grow in batch culture depends upon a number of factors, chief among them being the inherent maximum growth rate of the organisms, but other factors such as the nature of the medium, temperature and the availability of oxygen in an ærobic culture, are of great importance. The nature of the medium will be effective through the availability of the carbon and nitrogen supplied, the presence of necessary growth factors and trace elements, while the buffering capacity of the medium will affect the final amount of growth if there is any acid production. Shaking or mechanical stirring to keep the culture homogeneously mixed will also increase the rate of solution of oxygen in the culture and this will considerably increase the metabolic activity of the organisms with a consequent increase in the growth rate. However there will come a time when the medium is exhausted and the culture vessel will have to be cleaned out, sterilised, charged with fresh medium and re-inoculated. When a continuous process is employed, this turn round time and the inevitable lag phase that follows the inoculation of a batch culture are avoided and there is a consequent increase in the productive capacity of the culture vessel. Common examples of heterogeneous continuous biological processes are the production of vinegar and yeast, the digestion of sewage sludge, and the treatment of sewage by the activated-sludge process. However, the rate at which the organisms concerned in these processes multiply is small in comparison with the rates of which they are potentially capable. For example, the phenolic wastes from a coke works are treatable by the activated-sludge process without sewage with times of retention for the removal of the phenolic constituents of between 8 and 18 hr., whereas it has been shown that, by the methods of homogeneous continuous culture, mixtures of phenols and cresols can be metabolised by bacteria common to both processes, with theoretical retention times of 1·3-1·5 hr. (Ware and Evans, 1958).

The technique of homogeneous continuous culture has been developed from the early studies of such workers as Rogers and Whittier (1930), and Cleary, Beard and Clifton (1935). They failed to realise, however, that the technique was different from the commonly used methods of batch culture and that it was capable of using the reproductive capacity of the organisms to a much higher degree. Monod (1942) showed that in batch cultures the specific growth rate, that is the rate of increase of organisms per unit of organism concentration, is proportional to the substrate concentration when this is low, reaching a limiting saturation value at high substrate concentrations. He also showed that the weight of bacteria formed is proportional to the weight of substrate used and that this is a constant for a given set of conditions. These considerations were later applied to the practice of homogeneous continuous culture by Monod (1950), Novick and Szilard (1950) and others. With the development of the technique, there was a natural development of the theory behind it with notable contributions by Monod (1950), Novick and Szilard (1950a), Herbert, Elsworth and Telling (1956) and more recently with special regard to mutation and selection pressures, by Moser (1958). Only a brief summary of the basic theory need be given here.

Theory of homogeneous continuous culture

If a flask of culture medium is inoculated with bacteria, there follows a period during which there is no proliferation of the cells. This period varies in length depending upon the type of organism, the temperature of incubation, the state of the organisms at the time of inoculation, etc. This is known as the lag phase. There follows a phase of growth known as the logarithmic phase during which the bacteria multiply exponentially until a maximum viable population level is reached. The rate of growth is then equalled by the rate of death and the viable population is temporarily stable. This is the stationary phase. The rate of growth of bacteria in batch culture can be written as:

$$\frac{dx}{dt} = \mu x \quad . \quad . \quad . \quad . \quad (1)$$

where x is the number of bacteria

per ml., t is the time and μ the mean division rate.

But consider a vessel with a steady flow of medium and a constant overflow maintaining a constant volume. If the vessel contains non-proliferating cells, they will be diluted from the vessel at a rate

$$-\frac{dx}{dt} = Dx \quad . \quad . \quad . \quad (2)$$

where D the dilution rate $= \frac{\text{Rate of flow}}{\text{Vol. of vessel.}}$

When the cells are multiplying, the change in concentration of cells will depend upon a balance:

$$\text{Increase} = \text{Growth} - \text{Output.}$$

$$i.e.\ \frac{dx}{dt} = \mu x - Dx$$

$$= x(\mu - D) \quad . \quad . \quad . \quad (3)$$

Thus if μ is less than D, the cells will wash out more rapidly than they can reproduce themselves; but if μ is greater than D, the concentration of cells will increase to a level controlled only by some limiting factor, *e.g.* a nutrient, oxygen, *p*H, etc., at which point the rate of cell production will be equal to the rate of wash out, that is:

$$\mu = D \therefore \frac{dx}{dt} = 0$$

and a steady state is reached. Two forms of homogeneous continuous culture have been developed, the Turbidostat, and the Chemostat. In the former, all the nutrients are supplied in apparent excess and the population density is kept constant by the dilution rate. In practice this is done by a photocell which activates a relay when the culture density falls below a pre-set value. This stops the supply of nutrient until the density of the culture returns to its original value. This system is only suitable for laboratory scale experiments, but it is very useful for the selection of fast growing mutants. Bryson (1952) has used it for the selection of drug-resistant organisms. Variations of the apparatus have been described by a number of workers (Myers and Clark 1944, Anderson 1953, and Northrop 1954). The difficulty of preventing growth occurring on the walls of the growth tube, through which the turbidity of the culture is measured, has prevented experiments being continued for more than a few days. The theory of working of the Turbidostat has been shown by Herbert (1958) to be essentially the same as for the Chemostat.

In the Chemostat, growth is deliberately limited by a known and freely chosen factor, *e.g.* carbon source, nitrogen source, etc. The rate of growth will depend upon the concentration of the limiting substrate. If more of the limiting substrate is supplied, increased rate of growth is possible since as Monod (1942) showed, the rate of growth is related to the substrate concentration by the equation:

$$\mu = \mu\text{max}\left(\frac{s}{K_s + s}\right) \quad . \quad . \quad . \quad (4)$$

where K_s is the saturation constant which is the concentration of the limiting substrate at which the growth rate μ is one half the maximum possible growth rate μmax, and s is the concentration of the limiting substrate in the culture. This is shown graphically in Fig. 1.

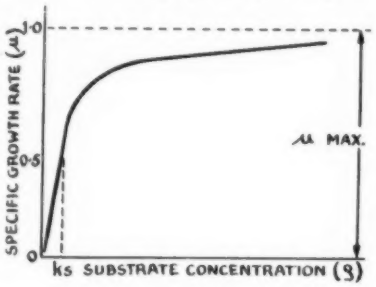


Fig. 1

Relation between exponential growth-rate (μ) and concentration of growth limiting substrate (s). K_s = saturation constant, μmax = growth-rate constant.

K_s is usually very small; forc arbohydrates it is of the order of mg/litre (Monod 1942), and for amino acids it is μgm/litre (Novick 1958). The amount of growth will be determined by the amount of substrate supplied and by the ratio of the weight of bacteria formed to the weight of substrate supplied. This is known as the yield constant Y:

$$Y = \frac{\text{Weight of bacteria produced}}{\text{Weight of substrate used}} \quad (5)$$

If this is known, it is possible to derive equations to define completely and quantitatively the behaviour of the culture. From equations (3), (4) and (5)

$$\frac{dx}{dt} = x\left[\mu\text{max}\left(\frac{s}{K_s + s}\right) - D\right]$$

and $$\frac{ds}{dt} = D(s_r - s) - \frac{\mu\text{max}\, x}{Y}\left(\frac{s}{K_s + s}\right)$$

where s_r is the concentration of the limiting substrate in the influent medium.

Then solving for

$$\frac{dx}{dt} = \frac{ds}{dt} = 0$$

the concentrations of organism (x) and of substrate (s) in the steady state, are given by:

$$s = K_s\left(\frac{D}{\mu\text{max} - D}\right) \text{ and } x = Y(s_r - s)$$

There are an almost infinite number of steady states obtainable over a wide range of dilution rates between the critical dilution rate at which washout occurs and the less well defined lower limit at which the cells cease to grow and go into a kind of lag state, only growing irregularly and sporulating if they can. Novick (1958) has stated that for a tryptophane dependent *E. coli* mutant (B/1, t) growing at 37°C., this lower limit is a generation time of about 15 hr.

It must be emphasised that for these high rates of growth to occur nearly perfect mixing is absolutely essential. This is essential for two reasons; firstly it ensures that the cells and the incoming nutrients are homogeneously dispersed throughout the culture vessel and prevents the aggregation of cells, and secondly, in an aerobic culture, it increases the oxygen-medium interface and so enables a much higher oxygen demand to be satisfied. On a very small scale, such as the Chemostat of Novick and Szilard, it is usually sufficient to bubble air through the culture tube at a fast rate, fresh nutrient being supplied to the culture through the air inlet tube. In larger scale apparatus, however, it is essential to have some form of mechanical mixing.

Various forms of Chemostat have been described by a number of workers for both laboratory and semi-industrial scale use. These range from the simple laboratory scale apparatus of Novick and Szilard (1950b) and Rothman (1955) among many others, to the more mechanised apparatus of Monod (1950), Perret (1957) and Elsworth *et al.* (1956), and to the semi-industrial scale apparatus of Monod (1950), Herbert *et al.* (1956) and Harrison (1958).

Applications of homogeneous continuous culture

By the very nature of its development homogeneous continuous culture has been studied mainly from the point of view of producing bacteria, studying their growth rates,

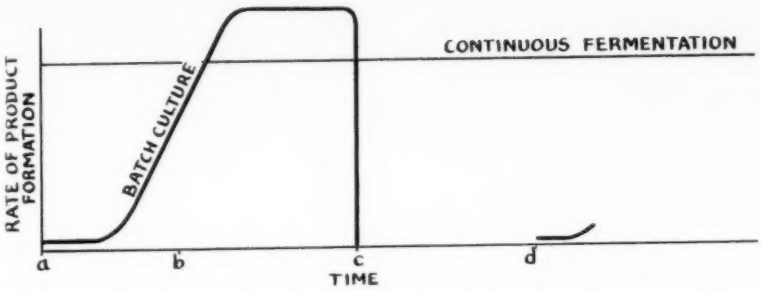


Fig. 2. Comparison of product formation in batch and continuous processes

mutation rates and general physiology. With a few notable exceptions, very few workers have considered that the technique has more than academic use. It is only recently that its potentialities have come to be exploited for the production of the metabolic products of micro-organisms, that have hitherto been produced by traditional batch culture. Pirt and Callow (1958, 1959a) have applied the technique to the production of 2:3-butanediol. In the first publication they describe a single stage process which showed that while the rate of product formation was increased three-fold, the concentration of the product and the yield expressed as a percentage of the theoretical yield was lower than that produced in batch culture. The use of a two stage process, described in the second paper, reconciled the conflicting requirements for growth and product formation; the cells were grown in the first reactor and were then passed to a second reactor where the production of 2:3-butanediol occurred.

Antibiotics

Antibiotics are at present produced by batch culture. Many of these are formed by bacteria, the Bacilli producing several, among which *B. subtilis* produces bacitricin, *B. brevis* tyrothricin, while nisin, used in cheese manufacture, is formed by some *Streptococci*. There is, it seems, no account of the production of these by homogeneous continuous culture although *B. megatherium* has been grown by Herbert (1958). But recently Pirt and Callow (1959b) have reported the successful culture of moulds by this technique. This had previously presented special problems, the hyphae tending to form clumps which prevent the perfect mixing essential to the proper working of homogeneous continuous culture. They describe the effect of *p*H upon the morphology of *Penicillium chrysogenum* and have shown that the resistance of the hyphae to shear, decreases with increasing *p*H to a point where pellet formation occurs. Since neither the formation of pellets nor that of long hyphae is desirable, they report that the *p*H optimum for growth of their particular strain of *P. chrysogenum* is *p*H 7. For the production of penicillin the optimum *p*H is 7·4 and this is therefore another case where a two stage process is indicated (Pirt and Callow 1959c). This has been made possible by the development of reliable methods of long term maintenance of *p*H under sterile conditions (Callow and Pirt 1956). It has also enabled organisms that previously had to be grown in batch culture because of *p*H variation, to be grown in homogeneous continuous culture and has made possible important fundamental studies of the effect of varying *p*H on the growth and behaviour of organisms.

Variation

Despite the possibilities of mutation and variant selection that are inherent in homogeneous continuous culture, it has recently been reported by several workers that organisms maintained under these conditions retain their characters more strongly than those maintained by serial transfer on solid or in liquid media. Finn and Nowrey (1959) reported that *Clostridium saccharoacetoperbutylicum* grown by exponential culture with a retention time of 45 min. showed less tendency to lose its ability to form butyl alcohol than did batch cultures. Similarly *Streptomyces griseus* has been reported by Perlman *et al.* (1954) to lose its ability to produce streptomycin after successive subcultures; Finn and Nowrey suggest that homogeneous continuous culture might prevent this loss. The apparatus used for this could be small and simple, requiring little maintenance.

Production of cells

Since it is possible by homogeneous continuous culture to produce very high concentrations of cells in large quantities, the technique is particularly attractive where the cells themselves are the desired product. It would thus appear very suitable for the production of vaccines, especially as the virulence of the cells is maintained. Bain and Jones (1958) have described the growth of *Pasteurella multocida* Type I (Roberts) in homogeneous continuous culture with retention times of 4 hr. for the production of hæmorrhagic septicæmia vaccines for cattle, with yields of up to 2 g. dry weight of cells per litre; but as yet, they have not tried to exceed running times of 5 hr. on a 44 litre scale and 48 hr. on a 10 litre scale. The vaccine made from these cells was shown to be as effective as that from agar-grown cells. Pirt (private communication) has shown that *P. pestis*, optimum growth temperature 28°C., has a full complement of antigens only at 37°C. Continued growth at the higher temperature induces a selection of organisms lacking various antigenic components, for example the immunologically important antigen 3. At this temperature the environmental *p*H also becomes important, for antigen 4, which is produced most abundantly at *p*H 6, is not produced at all at neutrality. A two-stage process with growth at 28°C. followed by antigen production at 37°C. with the *p*H controlled at 6·3 would result in the maximum yield of organisms and antigens with no unwanted selection. Similarly where the production of toxin is required, a second stage may well be necessary as the optimum conditions for growth may not be those for toxin production.

The production of baker's yeast is another example of a cellular product and is already being produced by homogeneous continuous fermentation by one firm in this country.

Production of enzymes

The production of bacterial and fungal enzymes is important to many industries, especially the food industry which uses amylases, proteases,

lipases and catalase. The pharmaceutical industry, in addition to amylases and proteases for digestive aids, uses streptokinase and streptodornase from Streptococci, for the destruction of blood clots and dead tissue. The production of dextran—a plasma extender—from sucrose by *Leuconostoc mesenteroides* (Bixler *et al.* 1953) is an example of a bacterial product of importance to this industry. Bacteria and moulds can be used for the production of many chemicals and are being increasingly used for the transformation of complex organic compounds such as steroids, which are being transformed experimentally by a continuous process. Homogeneous continuous culture methods have also been used for the production of Vitamin B_{12} and the production of beer. A most elegant application has been reported in the production of lysine and a patent has been taken out on the process by Pfizer Ltd. (U.S. Pat. 2,771,396). An *Escherichia coli* mutant is used to produce diaminopimelic acid which is then decarboxylated by a lysine independent strain of *E. coli* to produce lysine.

Food production

The search for supplementary food sources has led to experiments with the continuous production of algae and yeasts. The homogeneous continuous culture of algae presents special problems since light is essential for growth and will be a further limiting factor. Much of the work in this field has been reported by Burlew (1953), where an account is also given of the possibilities of using algae as sources of food and of raw materials such as protein and fats.

The culture of food yeasts has been mainly concerned with *Torula utilis*, reports of the work being given by Fencl *et al.* (1958) and Butlin (1958). Herbert (1958) described the growth of *T. utilis* in homogeneous continuous culture with generation times of 2 hr. or more and reported the variation of the amount of carbohydrate in the cells at different dilution rates in an ammonia limited medium.

Industrial potentialities

The industrial potentialities of micro-organisms are enormous and have been by no means exhausted, but it is obvious that speeding up the various processes in which they are used will have considerable importtance to manufacturers. It remains to consider the implications and the changes in current practice and thought that this would entail.

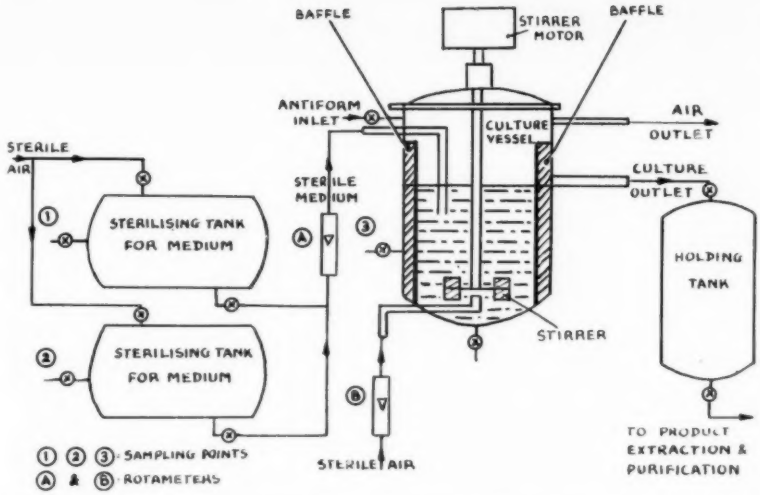
The maintenance of sterility in a batch fermenter is of the utmost importance in most fermentations and to ensure complete sterility is very expensive. In the case of a continuous homogeneous fermentation, the need for sterility precautions can be decreased in certain circumstances. The possibilities of contamination have been investigated by Powell (1958) and Moser (1958). Assuming that the invading organisms produce no substances that will retard the growth of the established population, the chances of successful invasion will depend primarily upon its physiological state at the time of entry to the fermenter and its growth rate. If, under the conditions prevailing in the fermenter, the invading organism has only a slight advantage in growth rate, the chances of it establishing itself are small. However, the continued infection of the culture by contaminants or mutants of higher growth rate must lead to their eventual success although they may not multiply for some infinite time. Thus the chances of contamination are smaller than in an equivalent batch process. As it is possible to employ a plant of the continuous type which is much smaller in size than that of a batch fermenter of comparable output, the cost of the initial installation can be smaller and money will then be available for the provision of sterility precautions and instrumentation, etc.

As the amount of air required in a homogeneous continuous culture apparatus will be smaller than for batch culture, the use of heat sterilisation of the air for an aerobic process will be made a feasible proposition. An elementary type of continuous heat steriliser for air has been described by Elsworth *et al.* (1955), for 1,700 litres per min., but this could be greatly improved by the suitable use of heat exchangers, etc.

A population growing in the steady state has no history and is unchanging, whereas a batch culture is continually changing. As there is a constant volume of output of constant composition, a culture in the steady state is amenable to automatic control; the recording of a single easily measured vector, such as carbon dioxide production, may be sufficient to indicate the performance of the culture. The use of an infra-red carbon dioxide analyser for monitoring a bacterial fermentation, has been described by Telling *et al.* (1958). They have shown how CO_2 measurement can be used to follow the production of sorbose from sorbitol in batch culture without recourse to other analysis. In the steady state, any change in the growth rate will be reflected immediately in the carbon dioxide analysis; this will act as an immediate warning and investigation can be made for a likely cause. This instantaneous response has obvious advantages over the analysis of the culture by other means which could well take hours or even days and it will also decrease the chances of contamination of the culture by sampling. There will of course have to be *p*H and temperature control with constant aeration and agitation rates implicit in the design of the fermenter.

The application of homogeneous continuous culture to a given fermentation will have to be investigated in each case. For example, several conflicting reports as to the possibilities of producing streptomycin in homogeneous continuous culture have been traced to slight differences in the conditions of culture, such as the presence or absence of zinc ions, the different behaviour of various strains and other unknown factors. The choice of limiting substrate best suited to a given product may warrant investigation for Rosenberger (1958) has shown that the production of lactic acid by *Streptococcus faecalis* in homogeneous continuous culture is increased by limiting the growth of the organisms by the nitrogen source—tryptophane—rather than the carbon source—glucose. The tendency for a culture to foam under the conditions of intensive aeration in the fermenter may present problems that need not necessarily be solved by the use of antifoams as these will also lower the oxygen solution rate and may therefore depress the performance of the culture. The development of continuous production techniques will require the parallel development of the continuous production of a constant medium and of continuous extraction techniques for harvesting the product such as that recently installed by Bowmans for the continuous extraction of lactic acid.

While there are many things to be considered and investigated before the decision to adopt the methods of homogeneous continuous culture is finally reached, it must be remem-



Hypothetical arrangement for continuous culture production unit

bered that the continuous use of plant leads to greater efficiency and economy. The time that can be saved is shown diagrammatically in Fig. 2. The time represented by a-b is virtually wasted from the point of view of product formation since this covers the lag following inoculation and the time taken for the cell concentration to reach a useful level for product formation. The time c-d is also time wasted as this represents the time taken for taking down the culture, cleaning out the fermenter, sterilising and refilling with fresh medium. Thus only the time represented by b-c is really productive, whereas with the continuous process, the level of product formation is constant represented by the straight line and can be at a level considerably higher than that for the peak production level by batch culture. Herbert *et al.* (1956) have shown that assuming a time of 6 hr. for the initial lag, final decline and turn-round time, if the doubling time of the organism is 2 hr., continuous production is 5 times that for batch methods and if the doubling time is only 30 min., then production is nearly 12 times that for batch culture. Thus it is evident that the advantages that can accrue from the use of homogeneous continuous culture methods are great and that there is world wide interest in the technique with understanding increasing almost daily; so that while it cannot be said that the technique has arrived in industry, it is arriving very fast.

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Friction and sparks. Every year the fire brigades attend over 1,000 fires caused by friction of one form or another. About two-thirds of these fires are attributed to over-heating of bearings and other parts of machines and the remainder to sparks from frictional impact or abrasion. About half the total of outbreaks occur in buildings and in an average year fires in the textile industry account for a large percentage of these, while fires in industries concerned with metal processing and machining account for a slightly smaller percentage. The remaining half occur in other places, often on storage sites, and mainly involve chemicals and explosives, rubber and flammable liquids.

The Fire Protection Association has now produced a Technical Information Sheet on the subject entitled *Friction* (*Mechanical Heat and Sparks*) (No. 5004). The range of sources of friction is considerable. Over-heating of bearings for example is to be found in a variety of conditions in which associated shafts, belts and other transmission units may play a part. These and various other sources of friction are referred to in detail; special attention is paid to friction in belts caused by undue tension. Where mechanical friction is concerned the remedy lies directly in good mechanical design and careful periodical inspection.

Copies of this booklet can be obtained free of charge on request to the Fire Protection Association, 31/45, Gresham St., London, E.C.2.

Air Conditioning—A Survey for Manufacturing Chemists

Air Conditioning in Vaccine Laboratories

In designing the air conditioning for the sterile suites of the Wellcome Research Laboratories, Beckenham, the problem posed was to create an acceptable local environment for the chemists and their assistants who work on the production of immunological preparations.

Each suite of rooms is designed for the performance of a particular process in the manufacture of a vaccine, anti-toxin or similar product. Access to the sterile rooms of each suite is through an anteroom, which opens on to a general corridor. Working clothes for the assistants are kept in the anteroom, and washing facilities are provided. The room is entered through sliding doors. In some instances the anteroom takes the form of a general laboratory which acts as a feeder to the sterile rooms.

The partitioning, benching and windows are designed to avoid ledges and inaccessible joints and wherever possible to reduce dirt pockets to a minimum. Unavoidable ledges are sloped at a steep angle to assist easy and efficient cleaning. Each room is cleaned down immediately before a run on a batch of the product. The assistants wear special shoes, gowns, headdresses and face masks.

The air-conditioning plant has to meet several conditions, *i.e.*

1. To maintain an acceptable dry bulb temperature at all times.
2. To prevent the moisture content (or relative humidity) rising above a certain level.
3. To maintain the suite at a pressure slightly above atmospheric.
4. To supply air to the rooms filtered at the highest possible efficiency down to half micron particle size.
5. To reduce to a minimum the possibility of cross-infection between plants serving other rooms in the same building.

These design considerations are met in the following ways:

1. An air heater battery is installed in the main supply duct to each suite, and the dry bulb temperture of the off-going air is controlled by a modulating thermostat in the return air duct. This results in a correct average temperature for all rooms of each suite.

A sterile room at the Wellcome Research Laboratories showing the air input and extract openings. Within the frames of the openings can be seen the terminal filters. Note that the extract connection is also filtered; this is done to ensure that, should the ventilation be turned off, any contamination within the extract duct will not fall back into the room. Normally the fan is run continuously to maintain the suite at a positive pressure.

2. A "Direct expansion" air cooler battery maintains the supply air at a controlled dewpoint by a modulating thermostat on the outlet of the battery. This thermostat adjusts the set point of a back pressure regulator fitted between the cooler battery (or evaporator) and the suction connection of the refrigerant compressor. The pressure regulator maintains a constant pressure (according to its set point) within the evaporator, and by this action and the resetting of its set point by the thermostat maintains the required dewpoint.

3. Sufficient fresh air, coarsely prefiltered, is admitted to the recirculating single fan ducting system to ensure positive outflow of air from the sterile rooms into the anteroom, and also to meet the fresh air requirement of the occupants.

4. The air is finally filtered at the point of entry to the rooms. No ducting is fitted between the filters and the rooms. The type of filter used is of the high efficiency paper type, having an efficiency rating of better than 99·95% against a methylene blue dust cloud. To restrict access to sterile rooms to a minimum the filters are housed in a special casing, so that they are changed from the plant space above.

5. All ducting is constructed with flanged joints between lengths and other joints are welded. Thus, infection between sterile plants in the same plant space and between these plants and other ordinary duct systems is made extremely unlikely. Each suite is served from an independant plant, comprising fresh air intake, cooler battery, heater battery, fan and refrigerant compressor. This provides flexibility on plant operation, and a breakdown on any one plant will not interrupt work in any other suites.

It has been found that the occupants require a comparatively low internal temperature for reasonable comfort due to the protective clothing worn. The design limits the rise in dry bulb temperature to 70°F.

with a dewpoint of 46°F. at maximum outside design conditions of 90°F., D.B. and 71°F., W.B. This is an "effective" temperature of 65°F. approximately. The internal dry bulb temperature is allowed to fall from 70°F. to 62°F. with the same dewpoint as the load on the plant decreases. This gives a minimum "effective" temperature of 60°F. approximately.

A cooling load exists throughout the year with the load varying between 100% to 35%. Precautions are taken on the refrigerant circuit to ensure that the compressor neither overheats nor induces sub-atmospheric pressures in the suction line and crank-case.

The plants were designed and installed by G. N. Haden and Sons Ltd., in collaboration with the chief engineer of the Wellcome Foundation.

Achieving Hospital Standards of Air Conditioning

THERE are obvious parallels between the standards of air conditioning required in hospitals and in pharmaceutical laboratories handling sterile products. The following notes have been extracted from an article on air conditioning in hospitals published by J. P. Sandison, B.SC., A.M.I.MECH.E., M.I.E.E., in the *Journal of the Institution of Heating and Ventilating Engineers* (1958, **26,** 209) and reproduced by permission of the Institution.

The air conditioning problem

The term "air - conditioning" should cover the complete control of the air state within the rooms concerned, and this entails:

(*i*) filtration for bacteriological purity;
(*ii*) control of dry-bulb temperature;
(*iii*) control of wet-bulb temperature;
(*iv*) control of air movement.

A degree of bacteriological purity and some control of air movement and dry-bulb temperature is obtainable with many conventional theatre plants, but complete control of wet-bulb temperature and consequently the relative humidity is obtainable only with refrigeration plant or drying agents, which considerably increases the capital cost of engineering work associated with air treatment.

There are few plants in existence in Britain or on the Continent which give complete control, but surgeons are becoming increasingly aware of the advantages of such control, particularly where lengthy operations are involved and where the comfort of the staff contributes to the success of such operations. A team of twelve persons may be working within a theatre and themselves contribute to a rise in dry-bulb temperature and relative humidity. Heat gain from these twelve may be in the order of 4,000 B.t.u./hr. and moisture gain of 1·3 lb./hr. These gains, coupled with high external wet- and dry-bulb temperatures during summer months in temperate zones and at all times in tropical and sub-tropical climates, do in the author's opinion fully justify the inclusion of refrigeration in the air-conditioning plant to give automatic control of the air state.

Design requirements

In considering the air-conditioning of an operating theatre in relation to medical requirements and to the results of recent bacteriological research, it would seem clear that design requirements should stipulate the following points:

(1) Clean filtered air to be introduced from outside the hospital building.
(2) Air to be automatically controlled to provide constant wet- and dry-bulb ambient temperatures in the theatre.
(3) To prevent the ingress of contaminated air from rooms surrounding the operating theatre a positive air pressure should be maintained within the theatre itself.
(4) To reduce concentration of bacteria released within the theatre from patient, dressings or theatre staff an adequate rate of air change should be maintained.
(5) To prevent, if possible, the movement of bacteria colonies from one part of the theatre to another turbulent air movement should be minimised.

Requirements (1) and (2) are met by many conventional air-conditioning plants, though, in the author's experience, efficiency of filtration is frequently haphazard. Dust particles down to 7 microns at least in size are considered a potential risk as carriers of infection, and whilst a fair degree of efficiency can be achieved with some types of paper or capillary water spray filters the author is of the opinion that maximum removal efficiency of really small particles can be achieved only with electrostatic-type filters.

Particularly in towns where high atmospheric pollution can be expected the electrostatic filter should be preceded by some form of coarse filter, preferably of a self-cleaning type. The electrostatic filter itself should not be of the metal plate type, which can present a risk in the event of current failure, but should have some form of filter medium upon which the charge is generated so that in the event of an electrical failure there is no serious carry-over of contamination from the filter itself.

An interesting reference to filtration and humidity control was made by Thomas Urdahl, an American consulting engineer, in a Paper given to the Summer Meeting of the Institution of Heating and Ventilating Engineers in June 1957. Urdahl was describing the use of desiccant driers using activated alumina. Not only does the activated alumina provide the necessary dehumidification but it also traps bacteria in the air passing through it, giving an almost sterile air state on leaving the unit. It is interesting to consider that modern practice in operating theatres has regarded recirculation as quite unsatisfactory from an air purity point of view. It may be, however, that if desiccant drying were introduced into an air-treatment plant some measure of recirculation might be permissible from the operating theatre itself without risk of cross-infection.

Requirement (3) presents problems which involve not only the engineering plant but the layout of ancillary rooms for sterilising, sluice, anæsthetic and X-ray purposes. Experience has shown that conventional air-conditioning plant, having separate air inlet and extract fans, cannot be relied upon to maintain a positive pressure within the operating theatre, even when fans of

a larger inlet capacity than extract are allowed. Variation in filter resistance, fan-belt slip, wind effect, etc., may influence the performance of the inlet system and may seriously reduce the designed level of positive pressure and indeed may reverse it, with consequent potential risk of contamination of the theatre atmosphere. Extensive experiments with a full-scale theatre model of the domed-roof type have shown it is possible to build up an air pressure within the theatre and to maintain it with a specified rate of air change when all openings to other rooms are closed. To achieve this without induced extraction by fans the air-inlet system has to be designed to maintain, on the type of room tested, an air flow with a room pressure equivalent to 0·04 in. to 0·1 in. water gauge. The pressure range was found to be fairly critical, as regulation below 0·04 in. was difficult to maintain and above 0·1 in. the effect of air pressure on the opening and shutting of doors became unpleasant.

Bacterial content of air

Requirement (4), dealing with bacterial content of air within the theatre, is difficult to satisfy. The removal rate of contaminated air which is completely mixed with incoming air follows a simple logarithmic law, where rate of disappearance of bacteria at any moment is proportional to the concentration at that moment. This law may be expressed as the convenient equation:

$$R = \frac{138}{t}(\log_{10} n1 - \log_{10} n2)$$

where R is the rate of air changes per hour and t the time in minutes between numbers of infected particles $n1$ and $n2$.

Airborne bacteria have a natural death and sedimentation rate which may be expressed as the equivalent of a rate of air change which can then be added to the clean air changes introduced. The result of this addition gives the total removal rate. For example, if the death and sedimentation rate for sneeze bacteria is five air changes per hour, as would occur in a room with no ventilation, and twenty air changes of clean air are added, then the contamination removal rate may be said to be equivalent to twenty-five air changes per hour.

Requirement (5), relating to movement of bacteria within the theatre, assumes considerable importance as a source of infection at the operating table, and it is probably true to say that the less the number of air changes in the theatre the more serious is the risk of infection from this source.

As already mentioned, bacteria are released by movement of theatre staff, from clothes, dressings, the mouth, nose and from dust present within the theatre. The stirring action of movement transmits such bacteria to all parts of a room with turbulent air velocities in the order of 20-60 ft./min. With any type of control of direction of air flow within a room it should be appreciated that unless velocity in the desired direction exceeds, say, 50-60 ft./min. these turbulent stirrings by movement of personnel cannot be prevented from distributing any bacteria present throughout the room.

If, as was the case in the model experimental theatre in question, a downward direction of air flow from ceiling to floor be selected, then, to maintain uniform downward piston-like motion of air at a velocity of 50 ft./min. would require some 300 air changes per hour—clearly an impracticable figure. It was realised, therefore, that air turbulence from movement of personnel would have to be tolerated, and after considerable experiment a rate of twenty changes per hour was selected as giving reasonable controlled downward air movement and rapid clearance of the theatre of contamination.

Curves prepared by Dr. E. J. L. Lowbury, after tests in the model theatre with a "slit" sampler at Birmingham, show the effect of clearance of bacteria released over the operating table with and without the ventilating plant running. Four minutes after peak contamination the concentration dropped, with ventilation on, to the low level of 10 colonies/cu. ft. Without ventilation, after 30 min. the concentration was still above 40 colonies/cu. ft. One of Dr. Lowbury's graphs indicates an interesting comparison in contamination at the operating table when the bacteria were released 6 ft. away from the table. With ventilation on, peak contamination at the table occurred after 5 min. and dropped within the next 5 min. to 10 colonies/cu ft. Without ventilation a much higher peak was reached in the first and the decay, after 30 min., dropped only to 35 colonies/cu. ft. These data clearly indicate the benefit of air change in controlling bacteria within the theatre, both at the table and away from it.

A further important factor found in course of tests on the model theatre was the influence of the jet effect of an entering air-stream from the inlet apertures in the theatre upon turbulent air movement within the room. Initial arrangement of inlets allowed for nine apertures only which, with twenty air changes, resulted in air leaving these openings at velocities of 250 ft./min. A final figure of 80-100 ft./min. was found best in relation to minimum random disturbance of the air content of the theatre.

The influence of wall and floor temperatures upon the movement of air within the theatre is considerable and, as already mentioned, research carried out by the Birmingham team has confirmed that cold theatre walls can produce a thermal movement which contributes appreciably to general air turbulence within the theatre.

A cold floor was not found to affect the air movement to a noticeable extent, but with the relatively high humidities to be expected in theatres a floor temperature below dew-point may be expected to cause some condensation with resulting slippery surfaces. This effect is normally confined to theatres at ground-floor level where the actual floor is in contact with solid ground. In many theatres, however, it is the practice to wash down the theatre floors between operations and a somewhat wet surface may, in any case, be expected. If a dry floor is to be ensured, then a floor-surface temperature not below 62°F. is recommended where theatre dry-bulb temperatures of 70-72°F. and a relative humidity of 60 per cent. are required. As a relatively small amount of heat is needed at a constant level, electric heating cable embedded in the floor and thermostatically controlled is a convenient and cheap source of warmth for this purpose.

General planning in relation to air treatment

In planning for positive-pressure air-conditioned theatres there are certain conditions imposed which dictate, to a greater extent than hitherto regarded as normal, the architectural planning and layout of rooms surrounding the theatre

and the construction of the building generally.

The design requirement of minimum air turbulence within the theatre necessitates low-velocity air input, which requires very careful design of ductwork with internal air guide vanes and large-radius bends. It will be appreciated that to accommodate the type of ductwork required there must be space available above the theatre ceiling to a greater extent than normal, and this would apply whether the domed or conventional square theatre is to be served. Whilst in the interest of maximum cleanliness it was decided to use open-ended inlet apertures lined with plastic and without grilles, the necessary degree of low-velocity air entry can also be obtained with special distributing grilles which impart a horizontal velocity to entering air and avoid a downward blow.

To maintain a positive air pressure within the theatre to prevent the ingress of airborne contamination from surrounding rooms, steps must be taken to provide clearly defined clean and dirty areas, with some form of air-lock to prevent direct opening of dirty areas to the theatres or sterilising rooms. The method decided upon by the Birmingham team, with which the author has worked, is to maintain an intermediate air pressure zone for anaesthetic room, sterilising room, access lobby and scrub-up area serving the theatre, with dirty areas such as the sluice room, access corridors and changing rooms, etc., at normal atmospheric pressure. Where the sluice room communicates with the theatre for receiving dirty instruments and soiled dressings provision is made for double air-lock hatches through which no air flow from sluice room to theatre is possible.

In practice, with an air pressure in the theatre equivalent to 0·06 in. W.G. the intermediate pressure zone would be stabilised at 0·04 in. W.G., the sluice rooms being at atmospheric pressure.

To minimise the possibility of transfer of sources of contamination from the intermediate zone to the theatre on door opening, it is further considered necessary to maintain approximately the same ambient temperature throughout the pressurised zones. Even with a higher air pressure in the theatre and consequent outflow of air on door opening, the thermal currents which can circulate with different room temperatures constitute a cross-infection risk—a fact commented upon by R. Bourdillon in his Paper upon "Infection of Clean Surgical Wounds" in 1951.

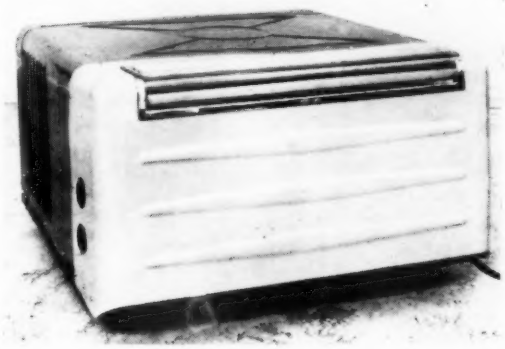
To avoid the adverse effect of cold walls upon air movement in the theatre it is convenient to arrange the planning in such a way that the room has the minimum of external wall construction and, where such walls are essential, to ensure that they are well insulated against thermal loss. Preferably the room should, from this aspect, have only internal walls and be entirely surrounded by other rooms warmed to a temperature close to that of the theatre itself.

Lighting

If this solution be adopted, there is then the problem of natural lighting to be considered. The degree of daylight desirable in theatres is a provocative subject. Some doctors consider daylight unnecessary in the theatre and others that it is essential. In the design under consideration the students' viewing portholes give sufficient daylight for normal cleaning tasks to be performed, and there are wall areas available near the X-ray viewing window and elsewhere for additional natural daylight if desired in particular schemes. In a theatre containing an outside wall windows introduced for daylight must be sealed against opening and should be double glazed with, in temperate climates, a warmed interior, to minimise thermal effect upon the desired air movement within the room.

A further factor influencing the structural design of the theatre and surrounding rooms for a pressurised air-treatment system is the need for many air-outlet openings which, for minimum turbulence, should be at regular intervals round the theatre walls near floor level. As these air outlets require control, in order that a positive pressure may be maintained within the theatre, it follows that a duct system must link the several outlets and that this duct system in turn must be controlled by pressure-sensitive dampers with discharge of exhausted air to outside the hospital building. In the design evolved by the team, special chimneys were provided for this purpose which, coupled with special automatic dampers, make an extract fan system unnecessary.

Self-Contained Units for Localised Air Conditioning



The Westool "105" model climatiser is designed to cool, filter and dehumidify the air in an area of up to 4,000 cu. ft. It can be easily mounted in a window or in an aperture in an outside wall.

Air conditioning of a pharmaceutical factory, particularly in the case of old buildings, generally involves an expensive and an elaborate tailor-made plant. In many cases it is an impractical proposition due to lack of facilities for duct runs and lack of central plant accommodation.

Quite often, however, only a specific aspect of production, *e.g.* the processing and storage of hydroscopic materials, required steady temperature and humidity, For example, the processing and storage of tablets and powders, which are very susceptible to temperature and humidity condition, present a special air conditioning problem. In such cases packaged type self-contained air conditioners can be used both effectively and economically.

A unit can be linked to remote thermostatic and humidistat control, and will deal with areas up to 4,000 cu. ft., depending upon conditions, and number of personnel. For larger

areas the unit is multiplied accordingly and zoned in the area concerned. Being self-contained this equipment can be mounted conveniently in a wall or window to atmosphere or to a conveniently open area. No ducting is required and the unit can be unobtrusively installed by local maintenance staff, and linked to standard electrical A.C. mains. One of the virtues of this packaged type of equipment is that the installation can be done by local labour, economically and quickly, at a convenient time, without any serious inconvenience to production routine.

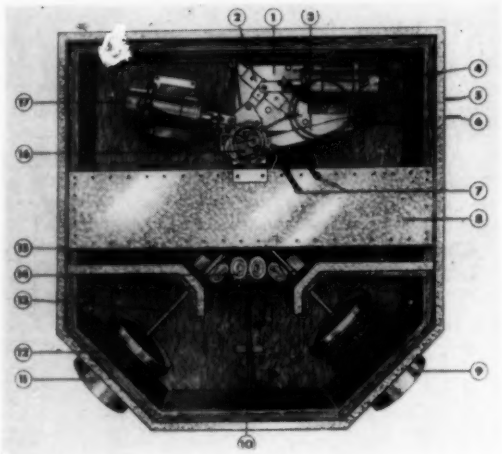
Where temperature conditions are reasonable and humidity is the major problem, particularly in the storage of powders, tablets and similar materials, then the more simple portable type dehumidifier can provide an efficient answer to the problem. These units are completely self contained, and portable, and can be placed in any convenient position in the room concerned. They operate on recirculation of air only, needing no contact with outside atmosphere. The excess moisture is extracted by low temperature refrigeration process and the water drained off into a container, within the unit, or to a drainage point. This portable type of equipment needs no ventilation whatsoever, and its highest efficiency is found in closed storage areas shut off from all outside climatic conditions.

Unit air conditioners are now being used successfully in a wide variety of applications in almost every industry. To the factory engineer, faced with specific problems of air conditioning, this type of packed unit offers a quick and rapid solution to many of his problems, where processes are breaking down due to unstable temperature and humidity conditions. By using individual units he can strategically place them where required and during periods of service, each individual unit can be dealt with conveniently, instead of shutting down complete plant and immobilising the general air conditioning and production of the factory.

In applying this self contained air conditioning equipment each application should be treated on its merits, and it is in the primary interests of the prospective user in the pharmaceutical industry to approach the manufacturer with details of his particular problem.

"Connor" Constant Volume Series 45 Valve Attenuator

1. Linkage mechanism
2. Linkage T member
3. Linkage volume control arm
4. Temperature control motor
5. Tube to thermostat
6. Tube to main pneumatic supply
7. Gauge connections for air delivery measurement
8. Sound attenuation baffle
9. Hot air inlet
10. Pickup for pressure regulator
11. Cold air inlet
12. Helical neoprene-coated spring damper
13. Damper push rod
14. Nylon pulleys
15. Stainless steel aircraft type cable
16. Pressure regulator
17. Constant volume control motor



Close Control of Air Conditioning

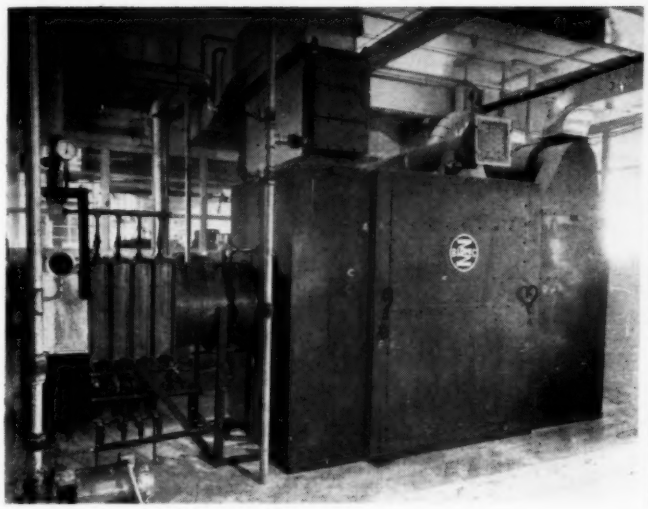
A high velocity air system, developed in the U.S. and now made in England, provides close control of air conditions and, furthermore, allows varying conditions to be obtained in adjacent spaces when supplied from one central plant. This is accomplished by a device called a high velocity valve attenuator. This provides desired temperature and acoustic conditions in each room served by a high velocity air-conditioning system, and maintains these conditions regardless of any alteration in the balance of the system caused by adjusting the controls in other rooms. Each room is under full individual control, although all the rooms are connected to the one system. The attenuators are available for single duct and dual duct systems. Single duct units have one inlet on the right hand or left hand side.

Dual duct units (see accompanying illustration) are furnished with a hot air inlet on the left hand or right hand side as required. The damper of the hot air inlet is open when the control pressure on the air motor is zero. The hot and cold inlets can be readily reversed in field. The dimensions, decibel ratings and static pressure characteristics are identical for single and dual duct units of the same size. All models are available with either flat plate or sinuous baffles. Static pressure taps for quick accurate air delivery measurement are provided on all models.

Constant volume control has been designed to produce uniform air delivery at all mixture conditions, despite static pressure fluctuations. Balancing the total air volume requires a single adjustment of the pressure regulator. The pneumatic motor controlled by this pressure regulator then actuates the volume control arm to maintain the air volume constant. The motors and pressure regulator are standard pneumatic control components for operation on air at a pressure of 15 p.s.i. The linkage mechanism may also be used with manual volume control instead of constant volume control (1 in illustration) when duct design permits. As this eliminates one air motor and the pressure regulator the cost is reduced. All valves have been designed to operate quietly. They are fully lined with $\frac{5}{8}$ in. acoustic material and equipped with an internal flat plate sound baffle. A patented sinuous baffle is added when exceptional silencing and best octave band distribution are necessary.

Adjustable air diffusers have been designed so that both the volume and the direction of air entering a room from a central air-conditioning system can be controlled from the room after installation. Many different types are available. Apart from standard units there is a combination supply-and-return unit, and units embodying lights and loudspeakers. Another unit has been designed to blend with acoustic ceilings.

The units are made by Ozonair Engineering Co. under licence from the Connor Engineering Corpn.



(Photographs by courtesy of Reckitt & Sons Ltd.

Left: **Birlec direct dehumidifier, model CO, and recirculation ductwork for maintaining relative humidities below 30% in air conditioned rooms at Reckitt and Sons Ltd.** *Right:* **Detailed view of tableting machine for hygroscopic powders at Reckitts showing complete freedom from clogging and caking due to the maintenance of relative humidities below 30%.**

Low Humidity to Suit Process and Workers

In pharmaceutical and fine chemical manufacture relative humidities in the range 25/5% are often necessary. They are most efficiently attained by the use of direct dehumidifiers which employ the principle of moisture adsorption on silica gel or activated alumina. Such installations, which operate at normal room temperatures, neither necessitate over-cooling of the air nor cause an undue increase in air temperature. The tonnage of refrigeration plant used in an air conditioning/adsorption drying system is insignificant compared with that required by a straight refrigeration system operating at the same relative humidity value.

Direct dehumidifier units are automatic in operation and regeneration of the silica gel or activated alumina is carried out automatically on one tray of the material, whilst drying takes place on another. The drying, regeneration and cooling cycle, which is designed to give the required dewpoint, is controlled by a special valve system operated by a timer. Depending upon the availability of a suitable service, the regeneration heat may be derived from electricity, steam, gas or oil. To save power when the room is not at maximum load, on/off control is provided. Air is thus enabled to bypass the dryer during the off period, yet maintaining air movement and temperature control.

Nearly 40 Birlec direct dehumidifiers are in service in the U.K. pharmaceutical industry. Whereas it is generally believed that adsorption drying is an economic process only for maintaining relative humidities at or below 25%, there are nevertheless several large systems in operation for maintaining humidities even up to 40%. The most usual application for the direct dehumidifier is in the tableting of hygroscopic materials. Such installations permit the continuous production of properly shaped tablets and ensure cleaner machines with less down time for adjustment. Many dehumidifiers are also used on rooms for the packing of hygroscopic liquids and solids: because of the dry atmosphere around the goods before sealing, quality is preserved and storage life is increased. Very dry air has also been found to be beneficial for low temperature sugar coating of pills and other heat sensitive products.

Contrary to common belief, the use of Birlec direct dehumidifiers for low humidity applications does not produce uncongenial working conditions. Indeed, the passing of air through desiccant material reduces the bacteriological count and helps to maintain a sterile atmosphere. On entering the conditioned space any sensation of chilliness, which is caused by clothing giving up moisture to regain equilibrium with the room conditions, rapidly disappears. Due to the consistent temperature and humidity levels maintained, many manufacturers have found the low humidity rooms to be the most popular and efficient working areas in the factory.

Portable Humidifier

Excessive dryness of air can be countered by a new portable humidifier. Apart from health considerations, dry heat can cause difficulties and financial losses during the storage or processing of materials (through differentials in weights or quality, reductions in tensile strength, increases in waste and dust, etc.).

Germicides, insecticides, deodorants, perfumes—can all be dispersed in the atmosphere with water, at the rate of up to one pint per hour, as micro-aerosols so small that they are completely " dry " in effect. The unit stands 10½ in. high, weighs 10 lb. and retails at £26 15s. It uses the same amount of electricity as a 60 watt bulb. Optional extras include time or humidistat controls, a neat stand, and a directional cowl for hospital use. Makers are Aerosol-Turbo Ltd.

Cleaning Air with Glass Fibres

The pharmaceutical industry is making increasing use of special filters for normal air conditioning and for prefiltering inlet air for high efficiency process plant filters. Fibreglass units of the R.50 and V.4 types are widely used for filtering air to laboratories, packing and filling rooms and office and factory working spaces. As prefilters in a high efficiency filtration chain they remove the bulk of particles from 5μ upwards, thereby greatly extending the life of the more expensive high efficiency units without greatly increasing the overall pressure drop.

The V.4 units have an initial resistance at 300 f.p.m. of only 0·07 in. w.g. and a collecting efficiency, measured in accordance with B.S. 2831, of 94% for 5μ dust. Being made from fine glass membranes they are both inorganic and non-hygroscopic so that foggy conditions cannot cause felting of the filter matrix. They are unaffected by most chemicals.

Fibreglass is also widely used in the high efficiency stages, usually in conjunction with steam sterilisation. Using deep beds of Fibreglass 2A fibre, tissue wool or staple fibre, or a combination of different fibre diameters, 100% sterile air has been achieved.

This complete filtration efficiency is vital for air supplied to antibiotic fermentation tanks and in the production of pure yeast and is usually obtained by steam sterilising the Fibreglass filter beds. A typical operating cycle is to continuously steam sterilise for a period of 2 hr. every seven days at 20-30 p.s.i. and 260°F. Under such conditions tissue wool has a life of approximately three months. The ability to stand up for such periods to the effect of steam without suffering mechanical breakdown is a function of the glass composition which is very carefully controlled.

The very high efficiencies mentioned are obtained either by judicious choice of packing density and depth for one of the Fibreglass fibre types mentioned or by using a combination of types to give a graded filter. Fibre diameters used vary from 1μ in the case of 2A fibre to 15μ in the case of tissue wool and the choice depends entirely on the operating conditions.

A third application for Fibreglass filtration material is metering. Here the wide range of densities and fibre diameters available has enabled a number of pharmaceutical firms to design equipment to meet their own special requirements.

The latest development by Fibreglass in the filtration field is the production of moulded slabs and cartridges in a variety of fibre diameters and densities which make replacement very much easier and, even more important, avoids the possibility of uneven packing densities which can lead to voids and channelling in deep bed filters packed by hand.

Bactericidal Radiation

The use of ultra-violet radiation for air sterilisation and deodorisation is based on the absorption of U.V. radiation by the nucleic acid which is the main constituent of bacteria. The radiation also changes the molecular structure of any matter suspended in air with the final—and most important—result that the nose can no longer perceive an odour.

The Buvan unit has been designed to produce a U.V. output possessing maxima in both the microbicidal and the ozonogenic range of wavelengths. The method of application depends on the layout of the plant and on the task the unit is required to perform. In the laboratory, "buvanised" air may be required in a small glass-walled cabinet for pathological experiments or batch production, and it is then that a unit is fitted within the cabinet. Similarly, one or a number of units will be mounted in a plant where, perhaps, one or two digesters or turbine driven separators cause a certain amount of offensive odours to pervade the air. Here, the Buvans would be fitted so as to irradiate directly the source of the odour, destroying it before it could reach other parts of the plant. Where the pollution is more general, and more concentrated, a collecting system consisting of hoods, ducting and fans will carry the malodorous air to an outlet. Under these conditions it will be advisable to interpose an irradiation chamber into the ducting just before the outlet and place the required number of units into it. The plant should be so designed that no part of the polluted air can possibly bypass the chamber in which deodorisation takes place.

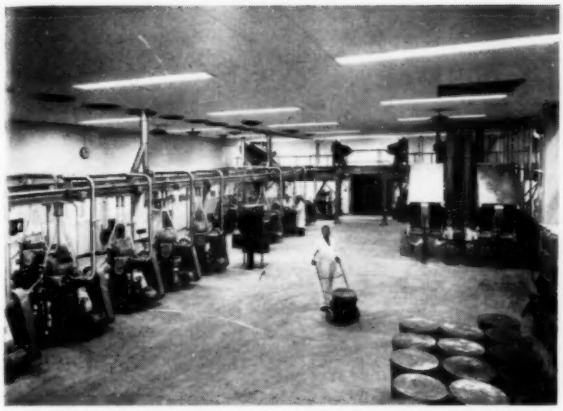
These are only the fundamental modes of using Buvan units and the experienced plant engineer will be able to devise many a variant particularly useful to his problem. As an instance it might be mentioned that Buvan units have been working for many years in a plant producing penicillin and other antibiotics; in a factory concerned with the lysing and processing of raw liver and producing vitamin B preparations; in sterile dispensing cabinets, etc.

As an approximation it may be assumed that one Buvan unit will control 5000 cu. ft. of air, depending on certain other factors. The electrical consumption of the monokymatic mercury vapour in quartz tube is 50 watt for an optimal output of bactericidal and deodorising radiation. The dimensions of the Buvan unit are 18 in × 5 in. × 7½ in., and its weight is just under 18 lb. This information was contributed by Barber Medico-Electronic Laboratories Ltd.

Pure Air for Aspro

The new factory for the tableting, packing, storing and dispatching of Aspro tablets at Slough has a production capacity of 8 million tablets a day. It provides first class internal working conditions independent of external environment and requires a very high standard of lighting, heating and air conditioning. Much of the production process was designed to avoid internal atmospheric pollution by dust, but the operation of the Manesty slugging machines, Stokes tableting machines and Aspro-Nicholas Sanitape and Sealtite packing machines called for special measures to maintain the exceptionally high standard of air purity required within the factory.

Dallow Lambert and Co. Ltd. were invited to examine the problems involved and after a considerable amount of development work were able to specify a complete dust control and collection system for the machines involved. By the use of close proximity hooding the tableting and packing machines were able to operate to the limit of their capacity with complete absence of dust emission. The contaminated air extracted from the machines is filtered and returned to the factory in winter and vented to atmosphere in the summer by Dustmaster unit dust collectors, situated in a plant room above the factory ceiling. These versatile units containing a



Left: **The tableting room at the Aspro factory with the dust control equipment fitted to the tableting machines. The packing machines similarly served are shown in the right-hand photograph; the extraction ducts rising from floor to ceiling are grouped together and clad with mild steel panels to give the appearance of structural columns.**

patent pad type filter element assembly, fan motor, dust container and automatic shaking assembly all within one unit chassis, have now been in operation for some months and require very little attention. The degree of dust control achieved with full production is exceptionally high and has resulted in many incidental advantages. The production of the tablet is improved and the frequency and running costs involved in cleaning the various machines and the factory walls, floors and ceilings are greatly reduced.

High Efficiency Air Filtration

Air filtration equipment has to perform many duties in the pharmaceutical industry. Apart from filters installed in general air conditioning and ventilating systems operating in offices and factories, there are certain special conditions that have to be met where personnel must be protected from direct or indirect contact with the products being manufactured. For example, dermatitis can be contracted through the discharge of fine powder into the atmosphere from a tablet processing plant.

For an application of this kind, Vokes have developed their " Absolute " range of filters consisting of models 33, 44 and 55. The 55 " Absolute " is used where an extremely high degree of filtration is required. The standard model has an element composed of special cellulose-based paper incorporating fine asbestos fibres. The paper is folded into a rectangular panel which is securely cemented into a wooden frame by a special resinous adhesive, which ensures freedom from leakage at the critical edge area. As the whole unit is manufactured from combustible material, toxically fouled filters can be easily disposed of by incineration. Efficiency against a methylene blue or di-octyl phthalate, dust cloud is better than 99·95% initially (*i.e.* 0·05% penetration). A special type has a penetration of 0·01%. Variants of the 55 include such types as high humidity, high temperature, flame resistant and high acid resistant panels and a model that is used where certain airborne bacteria is involved. A special housing has been developed for applications where viruses are handled and personnel must be protected against exposure to infection.

The 44 " Absolute " is an alternative to the 55 for special applications where a slightly lower efficiency can be accommodated but with a lower initial resistance. As a consequence, the life of the filter is extended beyond that of the 55 " Absolute." The filtering medium is basically cellulose fibres and a smaller number of fine asbestos fibres which allow for a greater porosity.

The 33 " Absolute " is similar in construction to the 44 and 55. It is used where asbestos fibres are undesirable. The medium in this filter is composed of special cellulose-based paper without asbestos fibres.

Working in conjunction with these high efficiency filters are usually prefilters such as the K.600 Kompak, Composite Kompak, Autoroll and Super-Vee. They help to protect the " Absolutes " by dealing with the coarser particles, thereby leaving the really fine particles to be handled by the high efficiency filters. K.600 Kompak and K.600 Composite Kompak filters can be arranged in bank formation for large air conditioning installations. These are ideal as main intake and extract filters or as prefilters to " Absolute " panels. Advantages include high efficiency, long life, reliability and extreme ease of maintenance.

The Autoroll is of the automatic type in which the effective area of fibrous filtering medium is disposed between two spools, the upper one containing the clean medium, the lower one the dirty medium. Passage of the filter medium from the top spool, across the air flow aperture and on to the bottom take-up spool is effected automatically by means of a geared motor drive caused to operate intermittently on a time cycle or a pressure differential switch. As the filtering medium is in the form of an expendable roll, it can be easily disposed of by incineration. Units of this filter can be bolted together to form a bank capable of filtering any volume of air.

The Super-Vee panel is an inexpensive, throw-away type of filter with a high sustained efficiency under severe " smog " conditions. It is unaffected by moisture, will not crack and is resistant to bacteria or fungal growth and meets the British Specification 476 for flame resistance. Panels can be supplied in metal frames where a greater degree of flame resistance is required. In various pharmaceutical applications these filters have been used with either " Absolute " filters or the Autoroll depending upon the conditions and requirements.

Air for Sterile Areas

By R. W. Rudin*

IN THE manufacture of antibiotics, vitamins and other pharmaceutical products, special techniques are adopted to ensure freedom from contamination by adventitious matter and in certain cases from micro-organisms. This is of paramount importance in the case of products used for injection therapy, but of less importance for products used, for example, for topical or oral therapy.

In the case of injection products the later stages of manufacture and the final filling into containers are carried out under conditions of the highest general cleanliness, and in particular it is necessary to ensure freedom from contaminating micro-organisms. This is achieved by the provision of sterile air-conditioned working areas. Wherever possible exposure of the products is avoided and the room atmosphere maintained at the highest possible level of sterility. Techniques which are in use to achieve this latter requirement are described below.

* Distillers Co. (Biochemicals) Ltd.

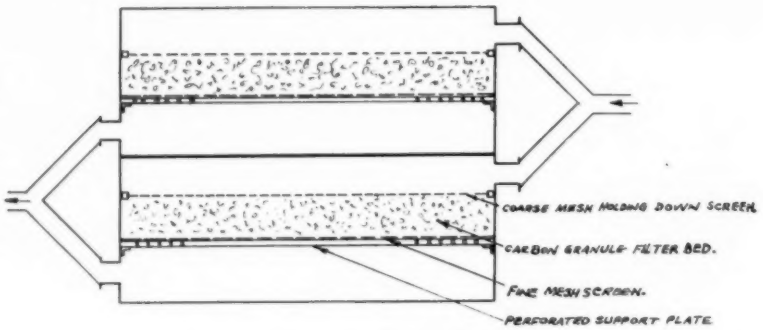


Fig. 1. Section of double tiered filter.

Early installations used chambers irradiated with ultra-violet light of wavelength mainly 2537 Å through which the air was passed. The output from a U.V. lamp can be expressed in power units of watts, and an approximate working figure of 20 watts per 1,000 c.f.m. of air was used, the relative humidity of the irradiated air being maintained at 50% or less for maximum bactericidal effect.

Later installations used carbon bed type filters. A typical filter consisted of a minimum bed thick-

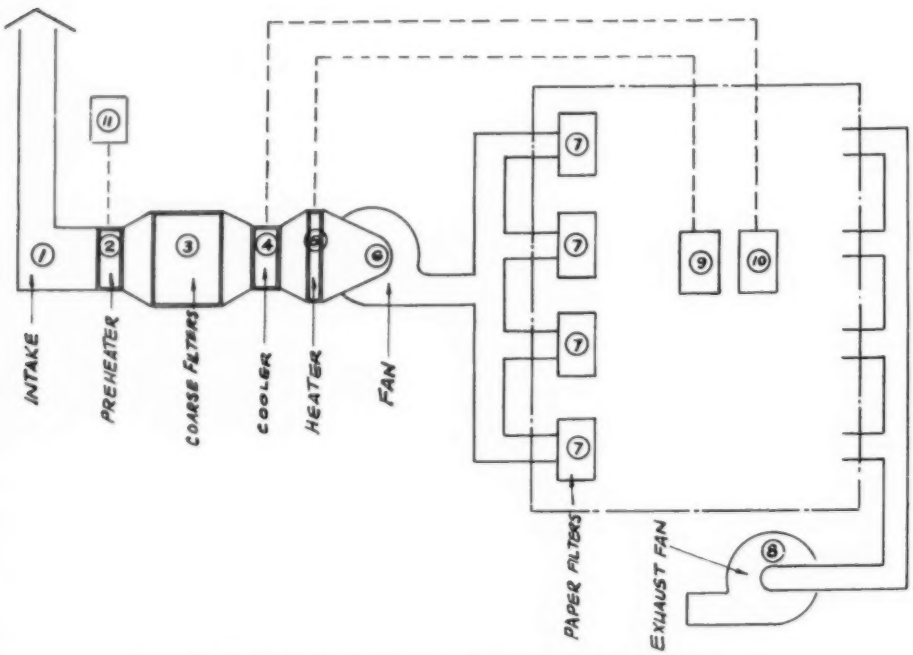


Fig. 2. Simplified schematic arrangement of air conditioning installation for sterile areas.

(1) Fresh air intake: At high level if plant location is dirty.
(2) Pre-heater: Steam or electric and automatically controlled to prevent freezing up of coarse filter or washer.
(3) Coarse filters: Cleanable or disposable type or cleanable screen and water washer type, or electrostatic precipitator. Removal of particles down to 5-10 micron size.
(4) Cooler: Finned tube or spray type. For temperature and humidity control. (Humidity requirements may necessitate absorption type drier or water injection.)
(5) Re-heater: Steam or electric.
(6) Supply fan: Axial flow or centrifugal.
(7) Terminal filters: "Absolute" paper type.
(8) Exhaust system: Naturally vented or assisted by exhaust fan. May be recycled to any point in supply fan intake system dependent on conditions for heating, cooling or filter economy.
(9) Temperature controller.
(10) Humidity controller.
(11) Anti-freeze heater controller.

ness of 6 in. of 8-14 mesh unactivated carbon granules with a maximum superficial air velocity of 0·5 ft. per second. Fig. 1 shows a diagrammatic section of a double tiered filter. The mechanism of this kind of bacterial filtration is not yet fully understood, but to be fully effective, water vapour in the air must be prevented from condensing out as airborne droplets and carrying impurities through. The pressure drop across this type of filter can be reduced by lowering the air velocity, but at the expense of increasing the filter area. This increases installation and periodic carbon renewal costs, but reduces fan operating costs, which must be carefully considered since the resistance of the typical filter described is approximately 10 in. water gauge when dirty.

Bacterial filters

Another development is the use of the so-called " absolute " type of paper filters with collection efficiencies of 99·95% of all sizes of dust pollution and a minimum collection of 99·75% of bacterial contamination. This type of filtration has a low cost in comparison with previous methods and lends itself readily to installation as terminal filtration, that is, the conditioned air leaves the filter directly into the clean area. Replacement of dirty filters becomes a simple matter and the difficulties of ducting " sterile " air are eliminated. Operating costs are very much lower with this type of filter than with carbon filters, the pressure drop being as low as 0·5 to 1·0 in. water gauge, using superficial air velocities of approximately 2 ft. per second.

Working areas are usually maintained under a slight positive pressure, about 0·25 in. water gauge, to prevent the ingress of unfiltered air, and although the risk of contamination is reduced as far as possible by meticulous steam, hot air or chemical sterilisation of all materials, clothing, etc., taken into a " sterile area," a final safeguard is usually provided by irradiating the area with ultra-violet radiation. Approximately 1 watt output per 100 cu. ft. of space has been found to be effective.

As a general rule " sterile areas " are kept as small as possible consistent with the apparatus and the number of operators required for operations such as filling of vials carried out under transparent enclosures. Operators wear gowns, head and face hoods, rubber gloves and vizors for protection against ultra-violet light, and since no great physical effort is normally required, 10 changes of air per hour are usually sufficient to maintain comfortable working conditions. At least 10 air changes per hour are considered advisable to minimise settling of such particles that are unavoidably carried in by operators, for example. The temperature and humidity are controlled at about 68°F. and 50% respectively, although the relative humidity may have to be controlled at a lower value when certain hygroscopic powders are being handled.

The general air conditioning, therefore, usually follows conventional procedure as regards movement, heating, cooling and distribution of the air. So far as possible, distribution of air within the working areas is arranged so that direction of air flow is from the product being handled towards the operating personnel.

Fig. 2 shows diagrammatically a typical simplified installation.

There are numerous ways of combining and arranging the chosen items of equipment required, but the bacterial filter is always in the last position before the conditioned air enters the area.

Advances in Cosmetic Formulation

Discussing modern trends in formulation at a recent meeting of the Society of Cosmetic Chemists, Dr. W. W. Myddleton chose a novel approach. Instead of giving a series of formulations he discussed raw materials and the way in which they have been altered to improve their cosmetic properties.

Thus, the search for germicides has led to the recently suggested use of triacetin in creams. This functions through the slow release of acetic acid by esterases normally present in the skin. Similarly, attempts have been made to reduce the unpleasant odour and irritant properties of formaldehyde by reacting with urea or substituted hydantoins to give products which slowly release free formaldehyde.

Unsaturated fatty acids suffer from the disadvantage of ease of development of rancidity, and it is interesting to note that linoleic acid urea adduct and also isopropyl linoleate do not become rancid.

Starches will withstand boiling with water after reaction with a tetramethylol urea acetylene compound and their resistance to bacterial attack is increased.

In the field of antiperspirants the gelation of aluminium chlorohydroxide solution by the addition of boric acid or borax in the presence of glycerine was mentioned and also the reaction of allantoin in the enolic form to give a 1 : 1 salt with aluminium chlorhydroxide. Liquid shampoo formulations in the past have presented the problem of maintaining clarity at low temperature without the danger of discoloration due to traces of iron when using the triethanolamine salt. Condensation of the lauryl alcohol with ethylene oxide prior to forming the alkyl sulphate leads to a product whose sodium salt has satisfactory water solubility at low temperature, is readily gelled and does not discolour in the presence of iron.

Dr. Myddleton then mentioned some of the apparent contradictions shown by some formulations. Silicones have many uses as antifoaming agents and it is surprising to find that they have been incorporated in shampoos with excellent results, giving good foam and having a conditioning effect on the hair.

Anionic and cationic surface-active agents, though normally regarded as incompatible, have been the subject of patent application for their use in equimolecular proportion in cream formulations as emollients and thickeners. Similarly the alkyl phosphate esters, though rather poor surface-active agents in comparison with the alkyl sulphates, are of value in emulsion formulation, the triester giving w/o and the diester o/w emulsions.

The unsatisfactory result obtained when using bisulphites followed by a bromate salt in hair waving is now claimed to have been overcome by the use of hexamethylene tetramine as " neutraliser " at a *p*H not lower than 6 in the presence of a trace of oxidising agent.

After answering several questions covering most of the topics mentioned in the lecture, the meeting closed with a vote of thanks to Dr. Myddleton for a most stimulating lecture.

Dr. R. H. Marriott was in the chair.

The Polyols—I

By Greville Machell, B.SC., PH.D.

The polyols are of great commercial importance, finding direct application as antifreezes and humectants. Among their derivatives, the ethers are often outstanding solvents, while esters find uses as plasticisers and explosives, and polyesters as surface coatings and textile fibres.

POLYOL is a convenient abbreviation of the full name polyhydric alcohol, which refers to aliphatic organic compounds containing two or more hydroxyl groups. There are literally hundreds of these compounds described in the chemical literature, and many of them, such as ethylene glycol, propylene glycol, glycerol and sorbitol, are manufactured on a large scale. In this article emphasis has been laid on the lesser known aspects of the polyol field, simply because much has already been written about the familiar compounds noted above. The simplest member of the polyol series is methylene glycol, $CH_2(OH)_2$. However, this compound has never been isolated and it is now generally recognised that compounds with two hydroxyl groups attached to the same carbon atom are incapable of separate existence, unless stabilised by an adjacent strongly electron-attracting group, such as formyl, —CHO, or trichlormethyl, $—CCl_3$.

Therefore we open with a description of the next member of the series, ethylene glycol.

Ethylene glycol

There are three commercial processes in use for the manufacture of ethylene glycol, two of which are based on ethylene and one on formaldehyde. The latter is little used, since ethylene is generally cheaper and more readily available than formaldehyde.

In the older, and more favoured, ethylene process, the ethylene is converted to the glycol through the chlorohydrin according to the following scheme:

$$CH_2 = CH_2 + HOCl \longrightarrow CH_2OHCH_2Cl$$
$$CH_2OHCH_2Cl + H_2O \longrightarrow CH_2OHCH_2OH + HCl$$

A continuous process is used, the ethylene being charged into a tower at 20°C. and 200 atmospheres together with a solution of hydrated lime. This mixture is then passed to the next stage where chlorine is added, and the chlorine reacts with the lime to give hypochlorous acid:

$$Ca(OH)_2 + Cl_2 \longrightarrow Ca(OCl)Cl + H_2O$$
$$Ca(OCl)Cl + Cl_2 + H_2O \longrightarrow CaCl_2 + 2HOCl$$

The ethylene reacts with the hypochlorous acid as indicated above, and the resulting chlorohydrin-calcium chloride solution is withdrawn for subsequent hydrolysis.

In the original method the chlorohydrin was hydrolysed directly to the glycol by adding the calculated amount of sodium bicarbonate, and heating the solution at 70°-80°. However, it has since been found advantageous to first convert the chlorohydrin to ethylene oxide by treatment with lime or sodium hydroxide:

$$CH_2OHCH_2Cl + NaOH \longrightarrow CH_2\!-\!CH_2 + NaCl + H_2O \quad (O)$$

since the ethylene oxide is a gas, and is then readily separated from the inorganic salts present in large amount. The oxide is then hydrated by treating with water at high temperatures and pressures in the presence of an acid catalyst. As the product is simply an aqueous solution of ethylene glycol, the latter is readily isolated by evaporation and distillation. The overall yield of glycol based on ethylene is in the region of 70%.

In the chlorination stage the formation of some ethylene dichloride is inevitable:

$$CH_2 = CH_2 + Cl_2 \longrightarrow CH_2ClCH_2Cl$$

and a second by-product, dichloroethyl ether, arises in the further treatment of the chlorohydrin. However, both of these compounds may be separated readily and recovered.

Recently, the catalytic oxidation of ethylene to ethylene oxide has achieved prominence, the oxidation being carried out with atmospheric oxygen in the presence of a silver oxide catalyst at about 300°:

$$CH_2 = CH_2 + \tfrac{1}{2}O_2 \longrightarrow CH_2\!-\!CH_2 \quad (O)$$

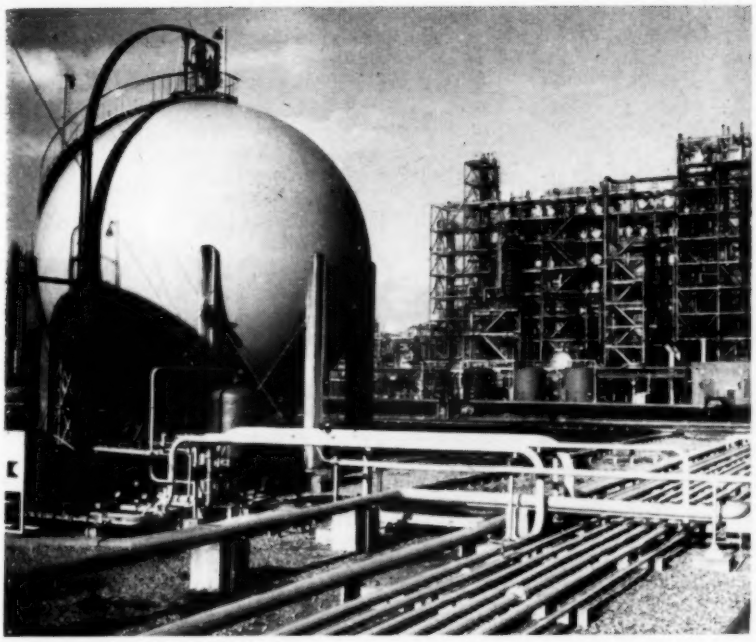
The oxide is then hydrated to give the glycol as described above, but the overall yield, at 50%, is somewhat lower, due to side reactions in the oxidation, which produce carbon dioxide and water.

The process based on formaldehyde is rather more complicated, and for success depends upon a cheap source of formaldehyde. In outline, this process involves three distinct operations: the production of glycollic acid, its esterification, and subsequent hydrogenation of the ester. Formaldehyde and water vapours are mixed with carbon monoxide, and the gases passed through a continuous reactor at 200° and 700 atmospheres. The glycollic acid produced is separated, esterified with methyl or ethyl alcohol, and the ester hydrogenated in the presence of a chromite catalyst at about 200°:

$$CH_2O + CO + H_2O \longrightarrow CH_2OHCOOH$$
$$CH_2OHCOOH + ROH \longrightarrow CH_2OHCOOR + H_2O$$
$$CH_2OHCOOR + 2H_2 \longrightarrow CH_2OHCH_2OH + ROH$$

The alcohol formed in the hydrogenation is returned to the esterification plant for re-use.

Ethylene glycol has many direct commercial applications, probably the best known of which is its use as an anti-freeze; it is also employed in the manufacture of transparent cellulose film and dynamite. The presence of two hydroxyl groups in the molecule suggests the possibility of polymerisation, and polyethylene glycols containing from two ethylene glycol units up to twenty are in commercial production. These compounds have the general formula $CH_2OHCH_2O\ [CH_2CH_2O]_x$



Ethylene storage sphere and No. 1 olefine plant main fractionating structure at the Wilton Works of I.C.I., in North Yorkshire

CH_2CH_2OH, and are hydroxyethers formed by elimination of water between hydroxyl groups. The polymers of low molecular weight are viscous liquids, while the high molecular weight compounds are wax-like solids. Polyethylene glycols are relative newcomers to the commercial scene, being used as rubber and mould lubricants, adhesives, textile sizes, and in cosmetics and pharmaceuticals.

The ethers and esters of ethylene glycol and diethylene glycol are of intense commercial interest. They are liquids of high boiling point, and are excellent solvents, particularly the monoethers. The latter are used as solvents for cellulose esters in lacquers, varnishes and paints, their lack of odour being a further advantage; they are also finding applications as hydraulic brake and shock absorber fluids in the aircraft and motor industries. Diethylene glycol monobutylether is used in the preparation of piperonyl butoxide, a synergist for pyrethrum sprays. Mono-ethers esterified with, for example, phthalic acid afford mixed ether-esters which are used as plasticisers.

Ethylene glycol is used in the manufacture of polyester resins, and this application has great potential for the future. Probably the best known product in this country is "Terylene," which is produced from ethylene glycol and terephthalic acid.

Propylene glycol

Propylene glycol, or propane-1, 2-diol, is technically available from propylene; the method of manufacture is analogous to that given for ethylene glycol, and will not be described further. Propylene glycol is also formed in the hydrogenolysis of sugars, and attempts have been made to find conditions under which a high yield of propylene glycol may be obtained. The most promising process yet described[1] utilises sucrose or glucose as the starting material, and this is treated in suspension in methyl alcohol with hydrogen at 250° and high pressure with a special copper-aluminium oxide catalyst. Under these conditions the initial reaction appears to involve reduction of the sugar to sorbitol (see later) and subsequent breakdown of this compound. Ideally, two moles of propylene glycol should be formed from each mole of glucose according to the outline equation:

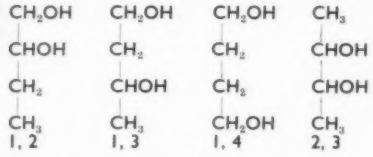
$$CH_2OH(CHOH)_4CHO + 4H_2 \longrightarrow 2CH_3CHOHCH_2OH + 2H_2O$$

but in practice the yield does not exceed 40% based on the glucose employed. Some glycerol is also formed, and under different conditions this may indeed become the major product, as described later.

Propylene glycol closely resembles ethylene glycol in many of its properties; several of the ethers are of commercial interest as solvents, and various esters and mixed ester-ethers are employed as plasticisers.

Butylene glycols

There are four positional isomers having the general name of butylene glycol, and the latter name, although widely used, is therefore ambiguous. The two hydroxyl groups can occupy the following relative positions:



but only the 1,4 and 2,3-isomers are of commercial interest at the present time.

During the second World War the Germans developed a process for the large-scale manufacture of butadiene from acetylene, in which 1,4-butylene glycol was an intermediate.[2]

In this process aqueous formaldehyde and acetylene are passed countercurrent over a metal acetylide catalyst under elevated pressure at a temperature of about 100°. The product is an aqueous solution of 2-butyne-1,4-diol, and when this is hydrogenated with a nickel-cobalt-manganese catalyst an aqueous solution of 1,4-butylene glycol (butane-1,4-diol) results:

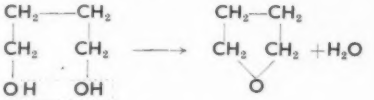
$$CH \equiv CH + CH_2O \longrightarrow CH \equiv CCH_2OH$$

$$CH \equiv CCH_2OH + CH_2O \longrightarrow HOCH_2C \equiv CCH_2OH$$

$$HOCH_2C \equiv CCH_2OH + H_2 \longrightarrow HOCH_2CH_2CH_2CH_2OH$$

In the above process a two-stage dehydration of the butane-1,4-diol then yields butadiene.

One of the attractions of this process lies in the alternative applications for the intermediate 1,4-butylene glycol. Dehydration of the latter in the liquid phase with phosphoric acid at 280°/100 atmospheres, affords tetrahydrofuran:



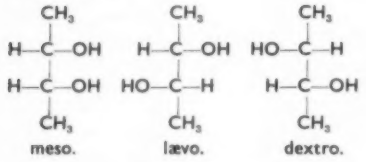
from which a large number of commercially important organic chemi-

cals are manufactured, for example adipic acid, γ-butyrolactone, N-vinylpyrrolidone, and derivatives of the hexamethylenediamines. The glycol is now being used directly as a cross-linking agent for polyurethane rubbers.

It will be noted from the above reaction scheme that the initial product from the acetylene-formaldehyde reaction is propargyl alcohol. Although its appearance in the isolated 2-butyne-1,4-diol can be largely suppressed by employing an excess of formaldehyde, some propargyl alcohol is obtained as a by-product. However, this highly reactive intermediate is disposed of to advantage, as is shown in a later section.

2,3-Butylene glycol (or butane-2,3-diol) has been known for 50 years as a product of the bacterial metabolism of various carbohydrates, and several processes have been suggested for its commercial production from molasses and other agricultural by-products of a carbohydrate nature. As 2,3-butylene glycol is also a possible source of butadiene for synthetic rubber manufacture, much attention has been devoted recently to production of the glycol by fermentation.[3] Under suitable conditions rapid and complete fermentation of molasses may be achieved giving 75 to 80% of the theoretical yield of 2,3-butylene glycol. It is important to carry the fermentation to completion, since this simplifies the subsequent isolation of the product from the medium.

Now 2,3-butylene glycol exists in three isomeric forms whose simplified plane structural formulae are noted under:



but it appears that the *meso* form is most generally obtained. Using *Aerobacter aerogenes*, a popular choice for the fermentation, considerable amounts of alcohol, lactic acid, and even acetoin, $CH_3CHOHCOCH_3$, are also produced.

Recovery of the glycol from the fermentation liquors is the most difficult and expensive operation involved in the commercial process. Vapour-phase extraction with superheated steam at atmospheric pressure gives very high recoveries, and

Glycol distillation column at the Carrington (near Manchester) works of Petrochemicals Ltd., an associate of Shell Chemical Co. Ltd. (Shell photo)

extraction with *n*-butyl alcohol also appears to be feasible.

The possibility of using 2,3-butylene glycol as an intermediate in the synthetic rubber industry was noted earlier, and both the *meso*- and the *lævo*-isomers can be converted to 1,3-butadiene. Direct catalytic dehydration gives very low yields of the desired product, ethyl methyl ketone being obtained instead. Pyrolysis of the diacetate, however, was reported[4] in 1938 and this has been further investigated by several workers.[5] Yields of *ca.* 85% may be obtained by passing the vapour of the diacetate through a tube heated at 575° to 600°C:

$$\begin{array}{l} CH_3CHCHCH_3 \\ \quad\;| \quad\;| \\ CH_3COO \;\; OOCCH_3 \longrightarrow \\ CH_2 = CH{-}CH = CH_2 + 2CH_3COOH \end{array}$$

The butadiene is of 99% purity, and the acetic acid may be recovered quantitatively for re-use.

2,3-Butylene glycol exhibits certain characteristics which suggest obvious direct industrial applications.[6] Its hygroscopicity and low vapour pressure can be utilised for moistening and softening such varied materials as glue, gelatine and casein, paper, tobacco and textile fibres. In these applications it would of course have to compete with established materials such as glycerol.

The presence of the two hydroxyl groups can be utilised for the production of polymers, such as those of the alkyd type. Esters, ethers and mixed derivatives are of potential value as solvents for lacquers and varnishes and also as plasticisers; certain esters with monobasic acids can be used in synthetic perfumes and flavours. Oxidation of 2,3-butylene glycol yields first acetoin and then diacetyl, $CH_3COCOCH_3$, which are highly reactive and versatile intermediates for organic synthesis.

Other dihydric alcohols

There are many other dihydric alcohols (diols) known, and several of these are commercially available, often from unsaturated hydrocarbons as in the case of ethylene glycol. However, only a few compounds under this heading are of sufficient interest to merit further description.

Among such compounds is pinacol, tetramethylethylene glycol, which is obtained from acetone by reduction. The obvious reduction product from acetone is isopropyl alcohol, but if the reduction is carried out under carefully controlled conditions, pinacol results:

$$2CH_3COCH_3 + H_2 \longrightarrow \underset{\quad\;|\quad\;|}{(CH_3)_2C{-}C(CH_3)_2} \quad \underset{OH\;OH}{}$$

The reduction may be carried out electrolytically or with a metal amalgam and acid.

The production of propargyl alcohol as a by-product in the manufacture of 1,4-butylene glycol was mentioned earlier. Oxidation of this highly reactive acetylenic alcohol gives 2,4-hexadiyne-1,6-diol, which on hydrogenation yields 1,6-hexylene glycol:

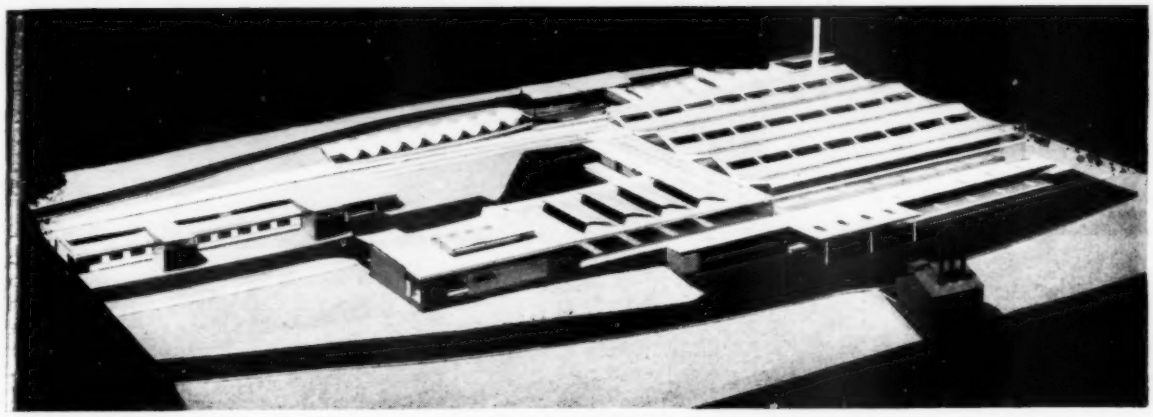
$$CH \equiv CCH_2OH + {}'O' \longrightarrow CH_2OHC \equiv C{-}C \equiv CCH_2OH + H_2O$$

$$CH_2OHC \equiv C{-}C \equiv CCH_2OH + 4H_2 \longrightarrow CH_2OH(CH_2)_4CH_2OH$$

A second hexylene glycol, 2-methyl-2,4-pentane-diol, has numerous applications as a solvent vehicle and humectant; it is also a constituent of hydraulic fluids, and a refrigerant liquid for industrial refrigerators and air cooling plant.

2 - Methyl - 2 - *n* - propylpropane-1,3-diol marketed under the trade name *Mepropol* is derived from 1-

(Continued on page 31)



Model of the £300,000 chemical works to be built by the chemicals division of Newton Chambers and Co. at Thorncliffe, Sheffield. On the left is the central laboratory block.

New Factory and Laboratories for Izal Products

AS briefly reported in our news pages last month, a new chemical works and a central laboratory block are to be erected for the chemicals division of Newton Chambers and Co. Ltd., Thorncliffe, Sheffield, at a cost of more than £300,000.

The present Norfolk works and the chemical factory at Thorncliffe—where *Izal* was discovered and developed in the last decade of the nineteenth century—are to be replaced progressively by a production unit incorporating the latest manufacturing plant and the most up-to-date methods of mechanical handling.

The new chemical works will also carry out for both home and export markets bulk filling of disinfectants, washing creams, insecticides, detergents, cutting oils, barrier creams, etc.

The whole redevelopment will take some two years to complete.

New dispatch bay

It follows naturally on the extensive reorganisation already in hand at the company's modern Izal factory. Here the premises are being extended and the latest automatic plant is being introduced. A dispatch bay with an area of 10,000 sq. ft., specially designed to serve both road and rail transport with palletised goods, is being built and provision is also being made for a further extension of 10,000 sq. ft. of production space to be brought into use as required to meet the growing demands for Izal products.

All this work at the Izal factory—including the introduction of improved systems for handling palletised goods—is already in hand, a natural preface to the bigger redevelopment scheme which will start in 1960 with the clearing of the site for the new chemical works.

Actual building will start in April and will proceed in two phases so that the production of Izal products will not be interrupted.

It is estimated that the main production section of the building will be completed by the end of 1960. Then during the first three months of 1961 units of plant and stocks will be moved to this section which will at once begin operating as a unit while other work such as the demolition of remaining buildings is undertaken.

In April 1961 the main building programme will be continued and the aim is to complete the entire project, with all its roadways and rail tracks and including the central laboratory, by the end of 1961.

Central laboratory

The central laboratory block will be important, housing the control, development, biology and works "labs" in the one building. The intention is to integrate the laboratories with the actual factory so that work can proceed in close contact with the problems of manufacture.

The new chemical works will be a functional building of clean lines, technically a single-storey factory with mezzanine galleries. It will be of steel Portal frame construction with external walls of engineering brickwork and extensive areas of glazing. Its overall area will be 92,500 sq. ft., with additional combined floor area for offices and laboratories of 9,620 sq. ft.

In providing the new manufacturing plant, the greatest possible use will be made of the technical knowledge of experts in the company's engineering division. They will contribute the know-how and most of the plant will be made at Thorncliffe.

To facilitate easy movement of road and rail traffic, the works is planned with a broad road approach linked to an extensive internal roadways system encircling the whole premises.

Future plans

Future expansion has been most carefully considered in the layout and internal planning of the works. Provision is made for the easy and economical extension of the main building as required and also for the extension of the receiving stores, offices and laboratories, so that the producing area could be doubled in size and yet still be served adequately.

The Works will be a pleasant place in which to work, having clean and colourful internal finishes with the minimum of exposed framing so that regular and economical redecoration can be undertaken.

PERFUMERY and Essential Oils

Perfuming ● Aromatic chemicals ● Lactones ● Gas liquid chromatography ● Rose oil ● Indian oils ● Agropyrene ● Vanilla

By A. J. Krajkeman,* Dipl. Ing. Chem., F.R.I.C.

Perfumes and perfume compounding

In a discussion on the purchase of raw materials for perfume compounding Cuttler[1] is of the opinion that " one must be very cautious in evaluating some of the claims now being made for the application of instrumentation." He ends by saying " . . . the reason for the product you use is odour, and the only way to detect odour is with your nose."

A similar subject, namely odour quality of an aromatic as opposed to its chemical purity has been discussed by S. Jellinek.[2] He poses the question which is so important to every perfumer, but even more so to every manufacturer of aromatic chemicals: What are we really looking for: a high-grade chemical or a good odorant?

The " Russian Leather " note can be produced in perfumes by a variety of aromatics, the most useful of which are certain phenols such as tert. butylphenol, tert. amylphenol, propenylphenol, carvacrol, thymol and similar products.[3] The use of these compounds is illustrated in an experimental formula for a " Russian Leather " base and in a number of formulæ using such a base in combination with other products.

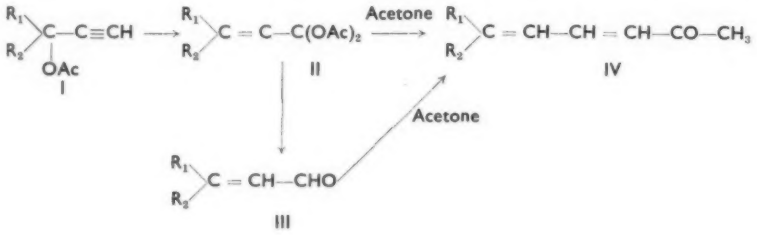
Perfumes in pressurised products are the subject of a paper by J. Pickthall.[4] After briefly dealing with certain problems of perfume compounding such as blending, ageing and fixation the author continues by describing properties and characteristics desirable in perfumes which are designed for application by spraying. A German patent[5] covers the preparation and use of *p*-bicyclohomofarnesol in perfumes. This alcohol is claimed to have a pleasant amber note which is stronger than that of the completely hydrogenated compound or of other unsaturated isomers. It is prepared from *p*-bicyclohomofarnesol by reduction with lithium aluminium hydride.

An article on the musk odour[6] is chiefly concerned with the olfactory effects produced by some indane derivatives. Patchouli oil, its preparation and composition, and its use in the perfuming of soap products is the subject of a review article which includes a number of perfume formulæ especially developed for soaps.[7]

* Söflor Limited.

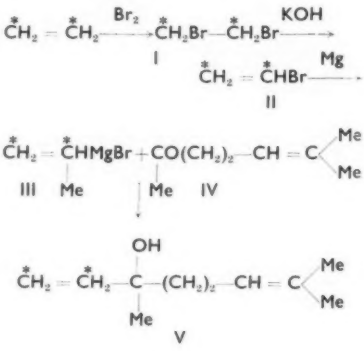
Synthesis of aromatics

A new method for the synthesis of citral and similar aldehydes as well as the preparation of ketones such as pseudoionones has been published.[8] Acetates of tertiary ethynyl carbinols (I) are rearranged to allenic acetates in the presence of acetic acid and a copper or silver catalyst. Partial conversion to diacetates (II) takes place under the reaction conditions. The acetates and diacetates are hydrolysed to α,β-unsaturated (III) aldehydes:



Treatment of the acetates with acetone gives $\alpha,\beta,\gamma,\delta$-unsaturated ketones (IV).

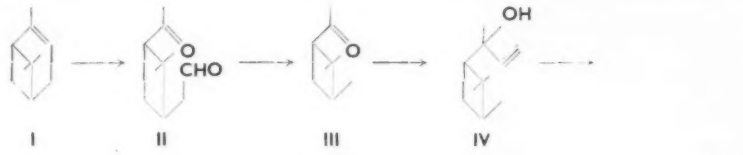
Dehydrolinalool was thus converted to citral and pseudoionone and methyl dehydrolinalool to methyl citral and pseudoirone in high yields. Linalool labelled with radioactive carbon was synthesised[9] by an adaptation of a method published by Normant in 1955. Labelled ethylene-(1 : 2 ^{14}C) was brominated and the dibromoethane (I) converted to vinylbromide (II) by means of caustic potash. This product gave with magnesium the Grignard compound (III) which was condensed with 2-methylhept-2-ene-6-one (IV) to give linalool-(7 : 8- ^{14}C) (V).



The labelled linalool will be useful in tracer experiments to follow the movement and transformation in plants of this alcohol as well as of geraniol, nerol, myrcene and other products made from it. Although squalene is, strictly speaking, not an aromatic, its chemistry is so closely related to that of terpenes that a new synthesis of this hydrocarbon is worth noting.[10]

A new synthesis of irones[11] has been developed recently from α-pinene (I). This hydrocarbon which

is obtained from turpentine is ozonised to cis-pinonic aldehyde (II). In the presence of a palladium catalyst the aldehyde is converted to a new ketone, pinonone (III). This ketone reacts with acetylene in the presence of sodium in liquid ammonia to give 3-(2,2,3-trimethyl-cyclobutyl) - but - 1 yn - 3 - ol (IV). On condensation with ethyl aceto-acetate cyclobutyl isomers of irone are obtained which have been named cyclobutirones (V). These react with 85% phosphoric acid to give a mixture of irone isomers (VI):



I II III IV

V VI

Naves has developed a method which allows the preparation of menthone from 3-menthane.[12] In a one-step oxidation-esterification reaction 3-menthene is converted to cis-*p*-menthane -3,4-diol by means of a hydrogen peroxide-formic acid mixture and subsequent hydrolysis with sulphuric acid. The mixture of isomeric menthones which results from this reaction is obtained in yields ranging between 57% and 76%.

Musk bodies are the subject of a paper which deals with the preparation and properties of benzene derivatives possessing a musk note.[13]

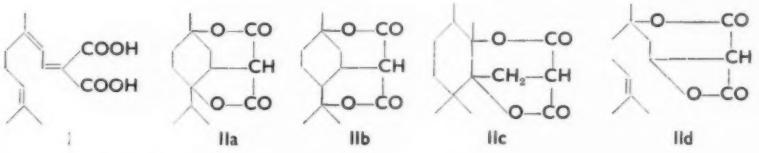
The chlorination of toluene normally results in a mixture of benzal chloride, benzyl chloride and benzotrichloride. Products chlorinated in the nucleus are also formed, so that benzaldehyde produced by the hydrolysis of benzal chloride always contains traces of chlorine. According to a patent claim[14] it is now possible to eliminate the formation of benzotrichloride and ring chlorinated bodies, and to reduce the proportion of benzyl chloride. This is achieved by liquid phase chlorination until not more than 35% of the toluene has been converted to benzal chloride. The reaction mixture is distilled to separate the benzal chloride from benzal chloride and from unreacted toluene. The pure benzal chloride is hydrolised to give benzaldehyde substantially free from chlorine.

The preparation of tertiary alcohols is the subject of a review article by Kulka.[15] Ten of the most important reactions leading to tertiary alcohols are outlined and examples of experimental conditions are given for each; 87 literature references are cited.

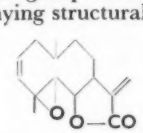
Lactones

When citral is condensed with malonic acid citrylidenemalonic acid (I) is formed initially. This compound rearranges on standing to a dilactone with one of the four possible structures IIa, IIb, IIc or IId. Structure IIb has now been assigned to this dilactone on the basis of nuclear magnetic resonance, infra-red spectra and the consideration of the compound's formation and decarboxylation.

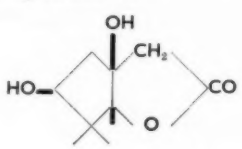
A sesquiterpenic lactone has been isolated from *Chrysanthemum parthenicum* (L.) Bernh. which has the formula $C_{15}H_{20}H_3$.[17] This lactone for which the name parthenolide has now been suggested is a ten membered ring with a γ-lactone and an epoxide group as shown in the accompanying structural formula.



IIa IIb IIc IId



When camphor is oxidised with Caro's acid to α-campholide, a by-product is obtained in a yield of 10-15%. This by-product has now been found to be a lactone with the following structure.[18]



Gas liquid chromatography

Gas liquid chromatography is being used increasingly in the solution of various problems in the field of aromatics and essential oils. For example . . .

Ylang-ylang concrete is the residue obtained after the removal of the solvent from the petroleum ether extract of ylang-ylang flowers. The absolute is that part of the concrete which is soluble in 95% of alcohol, six parts being used for one part of the concrete at a temperature of −15° to −20°. The composition of the concrete and the absolute was studied by Naves[19] by a method combining distillation, gas chromatography and infra-red spectroscopy. He found that the major constituents of the absolute are *p*-cresyl methyl ether, methyl benzoate, (-) - linalool, benzyl acetate and benzyl benzoate. Furthermore, he was able to prove that linalyl acetate and benzyl alcohol are completely absent, and that the presence of sesquiterpenes indicates adulteration of the absolute with ylang-ylang oil.

In a similar study of jasmine absolute[20] Naves has again not been able to confirm the presence of linalyl acetate. Absolutes of different origin were used for this work in which the value of gas liquid chromatography as a tool in this type of investigation has again been demonstrated. Naves has also found that the free linalool which occurs in jasmin absolute has only 80% of the optical activity normally associated with (+) − linalool.

The presence of linalool in Formosan citronella oil has been established by means of gas chromatography and infra-red spectroscopy.[21] It is found in the citronellal fraction of the oil.

Gas chromatography was also used to measure odours of foodstuffs.[22] For example, a sample of air taken from above the surface of an onion gave a useful chromatograph without the necessity of extensive sample preparation. Chro-

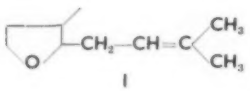
matographs of volatiles were prepared by direct sampling of cigarette smoke, beer, whisky, cheese, etc.

Many components of roasted coffee aroma were separated and identified by means of gas chromatography.[23]

An analytical method based on gas chromatography enables the isomers of ionones and methyl ionones to be determined.[24] Using Apiezon L on Celite as the stationary phase it is possible to determine the amounts of α- and β-ionones in commercial ionones, and also the α,β- and γ- as well as the δ-isomers in commercial methylionone.

Constituents of rose oil

Bulgarian rose oil is known to contain citronellol, geraniol, phenyl ethyl alcohol, linalool, nerol, farnesol, aldehyde C9, citral, benzaldehyde, eugenol, eugenol methyl ether and carvone. Five more constituents have now been isolated from the oil.[25] These are heptaldehyde, methylheptenone, *n*-hexylalcohol and an unknown oxide $C_{10}H_{18}O$. The latter has been found to be 3-methyl-2 - [3′ - methylbut - 2′ - enyl] - tetrahydrofuran (I).



I

Indian essential oils

Sphæranthus indicus is a medicinal herb which grows in India. On steam distillation a cherry red essential oil is obtained from it in a yield of 0·01%. The following products have now been identified in this oil:[26] Ocimene, α-terpinene, methyl chavicol, citral, geraniol, geranyl acetate, α-ionone, β-ionone (?) and α-cadinene. In addition two new compounds were found in the oil, a tertiary sesquiterpene alcohol and a tricyclic sesquiterpene. The structure of both these products is yet unknown, and the name sphæranthol is suggested for the alcohol, the hydrocarbon having been named inidcusene.

One of the most popular aromatics used in India is the oil distilled from flowers of the wild Kewda, *Pandanus odoratissimus* L.[27] The oil is obtained in a yield of 0·1 to 0·3% by extraction of the flowers with solvent, precipitation of waxes with alcohol and rectification of the oil in a vacuum. The odour of the oil is reported as being reminiscent of lilac superimposed on hyacinth and tuberose notes. Its main constituents is methyl β-phenylethyl ether, and it also contains dipentene, linalool, citral, phenylethyl alcohol and esters of terpene alcohols.

Japanese essential oils

Japanese peppermint oil is the main subject of a discussion dealing with essential oils and synthetic perfumes in Japan.[23] Tables of production figures are also given, showing weights and values of the different aromatics manufactured in Japan during 1956, 1957 and 1958.

Kenya essential oil production

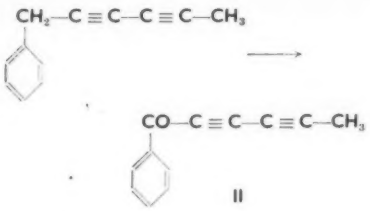
Dr. Guenther reports that the only two essential oils of importance produced in Kenya are mawah oil and geranium oil,[29] in spite of the efforts of Government officials and interested growers to raise a greater variety of oil producing crops. So-called East African cedarwood oil is also made, but only in small quantities as it is a by-product obtained in the manufacture of pencil slats and cedar board.

Methyl chavicol

Kam-Seh-Chang grass belongs to the *Araceæ* family and is found growing wild in the wet regions of Taiwan.[30] The oil obtained in a yield of 0·5% calculated on the freshly cut grass has not been previously investigated. Methyl chavicol has now been found as the main constituent of the oil which contains up to 95% of this compound. Since methyl chavicol can be isomerised to anethole which is not produced in Taiwan the author has studied the aspect of using Kam-Seh-Chang oil as a source of anethole which is highly valued in Taiwan as a flavour for a wide variety of commercial products.

Agropyrene

Treibs has investigated the oil obtained from the roots of *Agropyrum repens* L. (Triticum repens).[31] Rather surprisingly he has found only two constituents in the oil, namely 5% of carvone and 95% of a hydrocarbon to which he has given the name of agropyrene. This hydrocarbon is identical with the hydrocarbon capilene found by Japanese workers in *Artemisia capillaris* Thurb. and which was identified as 1-phenylhexadiyne -2,4 (I). The compound displays a remarkable antibiotic effect which, however, may be due to the ketone 1-phenylhexa - 2, 4 - diynone - 1 (II) which is readily formed from the hydrocarbon under the influence of oxygen.



II

Vanilla

Two very interesting and instructive articles[32,33] on the vanilla plant deal with the origin, historical development, production, marketing and uses of this important aromatic, which is also the subject of a discussion[34] dealing particularly with its application in the manufacture of alcoholic beverages.

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Pest Control Chemicals

By D. P. Hopkins, B.SC., F.R.I.C.

The £ s. d. of weedkillers • How nematocides work • Residues on tobacco • Mercury contamination • Pesticide research at Long Ashton • Fungicide protection of fruit in store • Weedkillers instead of ploughs • Bacterial insecticide

Weedkiller economics

A SURVEY and economic study of selective weedkiller use on wheat in south-east England is a valuable addition to the scanty literature on pest control economics.[1] To find out the extent to which MCPA, 2,4-D, DNC, etc., sprays are used on wheat two methods were used—interviewing area technical representatives of a major supplying company, and sending postal questionnaires to the district advisory officers of the N.A.A.S. for the area concerned. The survey by interview was more detailed than the survey by post, but on subjects common to both there were consistent replies. The year covered was 1954; delay in publication of results would seem due to the fact that the material has first been used for a thesis presented in 1958. Only wheat grown as a cash-crop on farms above 100 acres in farm size was considered.

Extent of use was assessed by the proportion of farms on which a selective weedkiller was given to *some* of the wheat acreage. The broad result obtained was:

Grouped farm size	*Percentage of farms on which weedkiller used*
(acres)	(%)
100-299	79
300-499	91
over 500	98
all sizes	83

Farms grouped according to yields of wheat (cwt/acre)	*Percentage of farms on which weedkiller used* (%)
10-19·9	44
20-29·9	90
30 and over	97
all yields	83

Farms grouped according to areas	*Percentage of farms on which weedkiller used*
North-East Fenlands	90
Eastern area	87
Central area	79
Southern area	72
all areas	83

The figures tabulated above do not show, of course, whether weedkiller is sprayed on half or more of a farm's total cash-crop wheat acreage. The proportion actually treated varies widely from farm to farm, but over half the respondents to the surveys estimated that *on average* 70 to 75% of the wheat crop per farm is treated. On the larger farms the trend is for the entire wheat acreage to be sprayed without regard to weed population variations between fields. It is deduced that about 60% (70-75% of 83%) of all wheat grown in the total area is treated with one of the selective weedkillers.

In the second section of the above table, the relationship between yields and use needs cautious interpretation. The yield differences do not entirely reflect effects of use or non-use. On farms where higher yields are expectable for other reasons there is greater certainty of income from wheat-growing and therefore more inclination to invest in the cost of weedkiller.

The paper provides a wealth of information about costs of treatment, but these costs vary with the weedkiller used, whether a low or high volume sprayer is used, and with the acreage sprayed per annum by a farm-owned machine. Also, the range of charges per acre by contractors is given. These data lead to a simple conclusion: that the cost of selective weedkiller treatment will not exceed 45s. an acre except when DNC is used for which the cost will be about 60s. to 75s. an acre. In many cases, except for DNC, the cost will be appreciably under 45s. an acre.

Does it pay to use weedkiller?

How does cost compare with benefits? There are two kinds of benefit—direct gain in yield, and what are called " non-yield " benefits. The latter vary in kind, but the most important is the greater ease of harvesting through reduced weed infestation. In addition there are such benefits as: cleaner grain sample, weed reduction for succeeding crops, saving of labour for other weed control attempts, earlier ripening, lower moisture in grain, etc. The survey information enabled these benefits to be ranked in order of importance as assessed by farmers' experiences.

The yield benefit has been estimated in weedkilling experimental work at gains of 3 cwt. per acre or 20-25% of the crop attainable without weedkiller use. The survey replies, however, put gains at a rather lower level. Over half the opinions put the gain at under 20% most opinions estimating between 10 and 15%. For farming practice, therefore, a yield gain of 12½% is assumed. With a non-use yield of 20 cwt. per acre, the gain is worth 75*s. an acre* at a wheat price of 30s. a cwt.

It is more difficult to assess the value of non-yield benefits, but the survey attempts this—estimating the value of ease of harvesting as 10s. to 35s. an acre, of cleanness of sample as 20s. to over 60s. an acre, and so on. The total value of these non-yield benefits is put at 75s. an acre except where a binder is used for harvesting when it is lower at 60s. an acre. The total value of yield and non-yield benefits is therefore 150s. to 135s. an acre, and this can be regarded as an average figure.

As the weedkiller and operation of applying it costs 45s. or less, or for DNC 60s.-75s., the gains of 135s. to 150s. are highly profitable. It is concluded that with quite low levels of weed infestation, selective weedkilling pays because of its low costs. As for the farms where so far these weedkillers have not been used the gains in yield would be above-average and the profitability of use would therefore be greater than the average indicated by the survey.

The paper is perhaps the first reliable assessment of the *practical* value of selective weedkiller. At a time when there is considerable and often ill-informed public comment about the use of " chemical " sprays on crops, it is a timely publication.

Nematocide activity

Little is known about the actual mode of action of nematocides such as methyl bromide, ethylene dibromide, and the newer substances such

as 1,2-dibromo-3-chloropropane or 1,3-dichloropropene. A common theory is that they exert a narcotic effect upon larvæ and that the effectiveness of these nematocides in soils depends upon vapour pressure, water solubility, etc. A new U.S. paper suggests[2] that there is a toxic effect due to reactivity, and direct contact-with-larvæ laboratory experiments have measured the concentrations of different organic halides required to produce 50% inhibitions of mobility. The concentrations found could be related to the chemical reactivities of the halides in the S_n2 reaction with potassium iodine in acetone. This suggests that the mode of action is possibly a displacement reaction with some essential nucleophilic centre in the nematode, *e.g.*, an amino- group in an enzyme system or in the protein or peptide system. The strong activities of some organic halides and thiocyanates support this speculation.

Two nematocidal substances do not readily fit this theory, however—allyl bromide should be more toxic than it is and 2,3-dichloro-1-propene should not be quite as toxic. The author explains this by presuming that other activity besides that shown by the S_n2 reaction with KI in acetone may be involved, such as the rate of hydrolysis and the toxic effect of the alcohol produced by hydrolysis.

Residues on tobacco

Residues of TDE (1,1-dichloro-2,2-bis(*p*-chlorophenyl)ethane) and endrin on tobacco have been studied[3] because these are the two insecticides applied in U.S. tobacco-growing at times nearer harvesting more than other insecticides. New sampling and testing methods were devised, and these showed that residues on green tobacco during priming exceed 50 p.p.m. for TDE and 10 p.p.m. for endrin. During processing about 45% of these residues are dissipated, most of this occurring in flue-curing. The loss is not larger because the residues tend to move during flue-curing into a slightly subsurface position and thereafter there is little further removal. Auction market tobacco still contains some 37 p.p.m. of TDE and 1·8 p.p.m. of endrin. The small consequent amounts of TDE and endrin in commercial cigarettes were measured—an average of 8 to 13 p.p.m. being found for TDE and 0·2 p.p.m. for endrin. For TDE rather more than a tenth of the residue in cigarettes was measured as entering the smoke-stream. It is suggested that the TDE or endrin residues in cigarettes could be greatly reduced, perhaps by more than half, if growers reduced rates of application and improved timing; this is known to be possible without loss in effectiveness of pest control. The work is uncompleted as there has so far been no study of the fate of residues in the inhaled smoke-stream; much or all of the TDE or endrin may be exhaled. The investigations have no doubt been prompted by the greater concern about connections between cigarette smoking and health.

Mercury residues

Mercury residues on harvested apples from commercial orchards sprayed with mercury fungicides are reported in a British paper.[4] The crops studied were those of 1956 and 1957. Samples were taken from orchards using phenylmercuric nitrate. The results showed that the mercury residue was below 0·01 p.p.m. in 29 out of 33 samples, and below 0·1 p.p.m. in the other 4. Only one sample, with 0·08 p.p.m. is regarded as possibly giving rise to concern. At this orchard a DDT miscible oil formulation was also used for codlin moth control and it is thought that this may have affected the persistence of the mercury. It is concluded that a 5-6 weeks interval between spraying and picking is adequate to reduce mercury residues to negligible amounts. Other work of recent date published whilst this research was being done[5,6] is mentioned. This broadly agrees with the results obtained.

Long Ashton research

The latest issue of the Long Ashton Annual Report includes, as usual, a number of papers on pest control substances and methods. Preliminary laboratory tests for new scab (apple) control chemicals have now been followed by field tests.[7] *n*-Dodecylguanidine acetate and phenyl mercury salicylanilide gave good results, reducing leaf scab by 84 and 83% respectively, and fruit scab by 87 and 72%; these degrees of control were secured without any signs of phytotoxicity. Both fungicides also seemed to check a light attack of apple mildew and to reduce red spider mite damage. In the same tests *o*-hydroxy-diphenyl and 2,4-dichloro - 6 - (*o* - chloroanilino) - *s* - triazine gave unsatisfactory results. The finding that *n*-dodecylguanidine acetate is so promising under British conditions is far from unimportant. In America this fungicide has already shown itself to be equal to and sometimes better than captan,[8,9] due it is believed to exceptional persistence of the sprayed material. This fungicide is known as *Cyprex*. The Long Ashton view is that two or three seasons' testing on a wide range of varieties are still needed before commercial use here can be recommended.

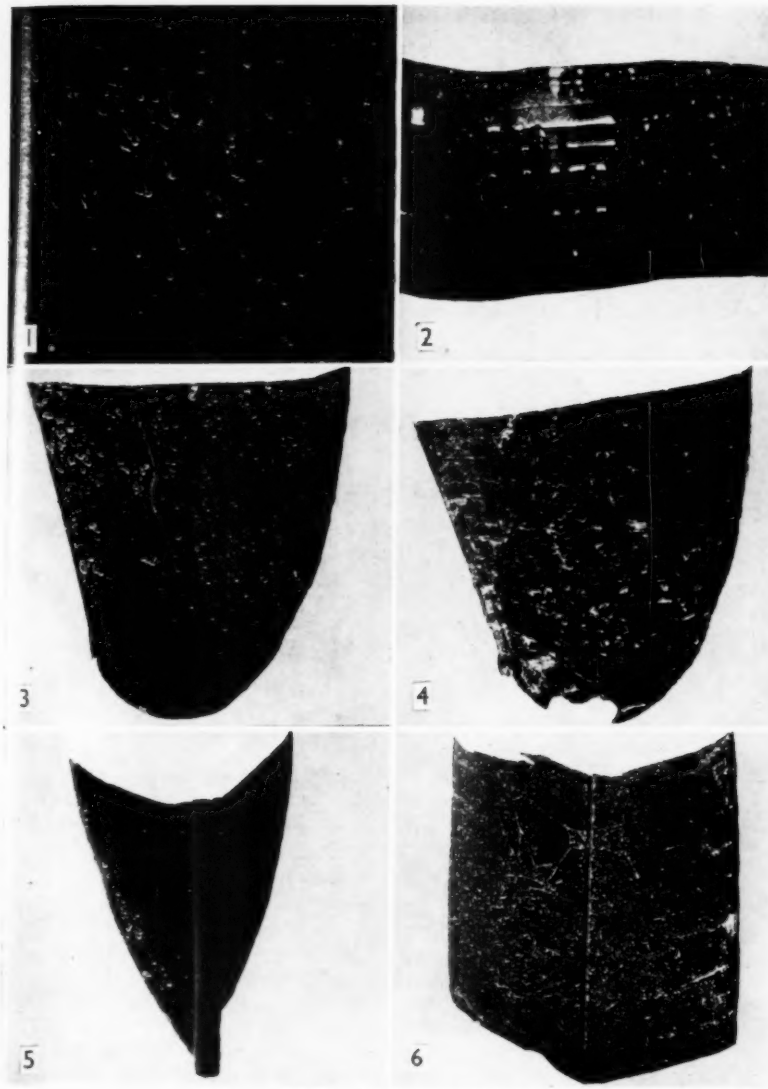
Another paper describes the use of fluorescent additives to sprays as visual indicators of spray coverage.[10] The additives used are Saturn Yellow and zinc 8-hydroxyquinolate. A quantitative estimate of spray deposition cannot be gained by this method in its present form, but it successfully compared spray coverages given by different kinds of equipment.

The phytotoxicity of surface-active agents used as wetters has been investigated.[11] A branched alkyl chain in the hydrophobic part of the molecule produces better wetting power than a straight alkyl chain. In any homologous series wetting ability rises with size of alkyl group. With non-ionic ethylene oxide condensates, maximum wetting is given by materials with the minimum number of ethylene oxides groups needed to create water solubility. Non-ionic wetters cause little or no phytotoxic damage with apples or plums. It is the anionic agents that cause damage and this is variable according to chemical nature and nature of leaf surface.

In homologous materials phytotoxicity increases to pass through a maximum as molecular size increases. This maximum usually occurs at fairly short lengths of the alkyl chain (dodecyl or under) so in effect phytotoxicity decreases as the alkyl group increases in size. This work, summarised in the Long Ashton Report, has appeared in fuller detail elsewhere.[12]

Fungicide use after harvesting

An interesting U.S. paper has shown that fungicide treatment may reduce the often sizable losses of fruit through rot during cold storage.[13] It is incorrect to attribute all loss to infections of the fruit when still on the trees; infection when the fruit is in the field boxes used during harvesting has been



Reproduced by courtesy of the Director, Long Ashton Research Station

Fluorescent deposits on abaca from various spraying machines. 1. Large drops, 2. Splashing, 3. Streaming, 4. Excessive cover, 5. Insufficient cover, 6. Adequate cover

indicated. These boxes are frequently re-used and tests have shown that they contain many different fruit rot pathogens. Apples and peaches, the latter being especially susceptible to rot in storage, were test fruits in experiments using fungicides to treat the field boxes. All fungicides employed reduced fruit losses appreciably, but the limited nature of the experiments makes it undesirable to draw comparisons between one fungicide and another. Fungicides used were: mercuric chloride, cycloheximide, copper sulphate, sulphur, captan, gluodin, maneb, zineb and amobam. With peaches the control of normally heavy loss was particularly striking. With one peach variety, spraying field boxes with captan reduced loss percentage 12 days after picking from 45% to 12%, and at 8 days after picking from almost 18% to only 1%. The cost of materials for treating field boxes is only 25 cents per 100 boxes. The value of fruit saved as indicated in this work may be up to 10-40 dollars. The paper, and a later discussion of its results,[14] may presage a new and highly economic field for fungicide use.

Weedkillers and pasture

A relatively new agricultural technique, recently described and discussed,[15] is the use of powerful selective weedkillers to destroy old swards in pastures and make it possible for new grasses to be sown without ploughing. This requires weedkillers capable of killing grass species, quick-acting yet not long-lasting. Among newer weedkillers TCA, dalapon and amino triazole may be considered. TCA is too slow acting and persistent. Dalapon has high toxicity to grasses if applied at sufficient rate, but it has a low toxicity for broad-leaved species. Amino triazole is much more toxic for broad-leaved species. Neither dalapon nor amino triazole are too persistent in the soil. The technique that has developed is to destroy the old sward with mixtures of dalapon and amino triazole or of dalapon and 2,4-D, preferably in autumn, following this by re-seeding in the spring. Experiments along these lines are cited, both in Britain and New Zealand. It is clear that this development, though to some degree promising, is still in the experimental phase.

The living insecticide

Last year in these Reports (see MANUFACTURING CHEMIST, April 1959, **30,** 161) the development of a new insecticide based upon the spores of a bacterium, *Bacillus thuringiensis* Berliner, was mentioned. This has been named *Thuricide*, and a new paper[16] reports upon extensive tests establishing its non-toxic properties for man, animals and plants. Mice, rats, guinea pigs and human volunteers were used in toxicity tests. In the human tests 18 volunteers orally consumed 1 g. of *Thuricide* daily for 5 days, and additionally 5 of the volunteers inhaled 100 mg. of powdered *Thuricide* daily for a similar period. Health remained good and this was checked by comprehensive medical examinations. Workers engaged in the manufacture of *Thuricide* were also checked during 7 months of exposure to the fermentation broth, the moist fermentation cake, the effluent and the final powder product. The two workers who had had greatest time of exposure kept in excellent health and examinations revealed no chronic or acute reactions. The animal

tests similarly revealed non-toxicity. Other tests referred to in the paper have included laying hens, chicks, pigs, fish and bees. A fear that this bacterial-based insecticide might not be as harmless as first claimed has arisen from its morphological kinship with *Bacillus anthracis*. It has been speculated whether a mutation could change the spores of *Bacillus thuringiensis* into the virulent spores of *B. anthracis*. No contamination during production, or other cause, has brought about such a change in 2½ years. In any case, no batch is released for handling and use until it has satisfied a safety test with mice.

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CASTOR WAX PROCESS

Experimental work, by M. Zajcew of Engelhard Industries Inc., Newark, N.J., U.S.A., on the hydrogenation of castor oil using a palladium catalyst, is said to have given a satisfactory wax product, obtained under what are stated to be "extremely mild working conditions, which would permit important operating economies." Operating costs are said to compare favourably with processes using a nickel catalyst.

The product obtained was a good quality castor wax and was prepared at 100°C. and 45 p.s.i.g., using a modified palladium catalyst. The wax nad an iodine value of 4, a hydroxy value of 145, an acid value of 1·8, and a capillary melting point of 86°.

BOOK REVIEWS

Industrial Fatty Acids

and their Applications. Edited by E. Scott Pattison. Reinhold, New York, 1959; *Chapman and Hall, London. Pp.* 230.

WITH the changeover from soap to synthetic detergents, a surplus has resulted of tallow and other sources of fatty acids. A new industry has developed producing narrow cut or even pure fatty acids which, while at present more expensive than fats, offer advantages for improved materials. The absence of glycerin and acids with undesirable properties for the particular application are particularly important in the manufacture of plasticisers and copolymers. Speciality soaps made from narrow-cut acids are free of the lower molecular weight products which cause skin irritation. This book is therefore timely in suggesting potential markets to fatty acid manufacturers. It gives an outline of the various industries utilising fats and fatty acids. Members of the Fatty Acid Producers' Council, whose chairman is the editor of this book, have collaborated to produce 16 separate articles under the above title. Apart from the introductory chapter by Pattison, the others are all by specialists in their own fields. The result of such a work is a difference in presentation of each chapter, but in general they are all well written and easily readable, giving technologists and executives a clear picture of each subject covered. One exception, perhaps, is chapter 14 on "Polymers of Vinyl Esters," which is a literature survey of the type frequently found in American journals, where each sentence is a reference. Three chapters dealing with production methods of fatty acids are well illustrated with flow sheets and photographs. A table showing composition of tall oil appears on p. 35; it would have been useful if similar tables on tallow and vegetable oils were included in the appropriate chapters. The chemistry of "Cleavage Processes" (chapter 5) is very well written, as is the following chapter on "Chemical Reactions." The chemistry of esterification processes is covered in detail, explaining the difficulties involved. Other reactions of no commercial interest at present may offer ideas to chemists for new applications.

An objection is felt on reading chapter 8 on "Metallic Soaps," where HFA and MeO are written for fatty acid and metallic oxide respectively (pp. 101-3). Many of the articles include tables of production statistics which exhibit some very interesting results. No one industry uses more than 15% of the total fatty acid production. Synthetic detergents still utilise a large proportion of fatty acids as esters of glycerol, glycols and sorbitol, and more than 50 pages have been devoted to this subject contributed by three authors (chapters 11 and 12). It is surprising that nowhere in the book is there mention of antioxidants to preserve colour and odour of fatty acids. The chapters on "Handling and Storage" (15) and "Test Methods" (16) will be invaluable to those in the consumer industries. Duplication of statements by individual authors has been avoided as far as possible by means of cross-references to the appropriate chapters.

L. RAPHAEL.

Phosphorus and Its Compounds

Vol. I, Chemistry. By John R. Van Wazer. Interscience, New York and London, 1958. *Pp.* 954.

THIS is the first of a two-volume work. The second volume, now in preparation, will cover the technology of phosphorus compounds. For a textbook of this type it is remarkably well written in an easy style so different from, for example, Mellor's "Treatise on Inorganic Chemistry." The author specifies that this is not a treatise, for such would cover several volumes. It is, however, an essential book for all chemists who utilise phosphorus compounds. The properties of about 500 compounds are discussed and there are 1,500 references.

The wave mechanical theory has been used throughout to explain structures without burdening the reader with mathematics. In fact, it is only in chapter 12 that some mathematical expressions are used

to explain the statistics of random reorganisation in condensed phosphates, and even these few pages (734-44) will not frighten the uninitiated.

Phosphorus shows similarities to its neighbours in the Periodic Table including carbon. The most stable compounds contain quadrivalent phosphorus atoms, by means of sp^3 hydbridisation. Even those which empirically appear to contain trivalent or pentavalent phosphorus, *e.g.* P_2O_5, have this structure in which P is attached to four oxygen atoms, three of which are shared.

About half the text deals with the various phosphates on which much light has been thrown in the last decade. The Appendix lists 187 mineral phosphates, including over 40 apatites. This wide distribution is due to migration of other elements into the apatite structure. The numerous condensed phosphates form polymers with rings or chains or both, showing resemblance to silicon or carbon polymers. Time and temperature are governing factors whereby the ration of P_2O_5 to water or metallic oxide, as well as the structure, establish a whole series of phosphates with different properties ranging from viscous liquids to solid glasses. The glasses are commercially important because of their high U.V. transmission and inertness to fluorides.

Nomenclature of the lower oxyacids was agreed by a committee in 1952. Although the author has used this terminology, he strongly criticises the system as being illogical.

A few small printing errors have occurred. On p. 690 "considerably" should read "considerable"; at the bottom of p. 777, $NaCO_3$ for Na_2CO; pp. 790-1 "stearic" in place of "steric."

L. RAPHAEL.

The Sequestration of Metals

By R. L. Smith, Chapman and Hall, London, 1959, *Pp.* 256, 42*s. net.*

DR. SMITH provides a general exposition of the theoretical and practical aspects of sequestering agents. He fills the gap that exists between original papers on the one hand and manufacturers' literature on the other, and he writes lucidly and critically. The book is addressed to graduate chemists who have no specialised knowledge of the subject and to whom sequestering agents would be a useful supplementary tool in their study, research or employment.

Five chapters are devoted to theoretical considerations under the headings: Definition of Sequestration. Valency and Basicity, the Chelate Ring and the Influence of Ligand and Metal on the Strength of Bond, Stability of Chelates and Competitions in Chelate Systems, and Chemical and Physical Properties of Sequestering Agents. It should be noted that the book is not only concerned with relatively new compounds like E.D.T.A. and other amino-carboxylic acids, but with compounds like the polyphosphates, the hydroxy-carboxylic acids, and other materials included in Dr. Smith's definition of sequestration as being "the suppression of a particular property of a metal in solution, without the removal of that metal either into another phase, nor its concentration into a particular portion of the original phase," the sequestering agent also not introducing any change into the system to make it unsuitable for the original purpose.

A chapter on general considerations in the application of sequestering agents serves as introduction to 15 sections arranged according to industry of use. This includes 3 pages on applications in the cosmetic and pharmaceutical industries, where 31 references and 20 patents were noted, mainly relating to E.D.T.A. These are in addition to the numerous applications of E.D.T.A. in pharmaceutical analysis due to Budesinsky and others, which are only partially covered in the chapter on analytical chemistry. In this section it may be noted that the original work in the application of a redox indicator in E.D.T.A. titrations, due to Brown and Hayes, is not included in the references quoted.

Other applications allied to the pharmaceutical field, such as stabilisation of drugs by E.D.T.A., are described in the section on applied biology, which has become the most extensive field of application of E.D.T.A., with numerous references quoted. A final chapter discusses possible future developments in the field of sequestration.

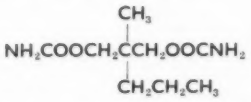
There are several minor misprints in the book, but they do not detract from the notable service that Dr. Smith has performed for workers in this field.

E. G. BROWN.

THE POLYOLS

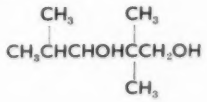
(*Continued from page* 22)

methylvaleraldehyde and is used in the manufacture of the tranquillising drug, meprobamate. This is the carbamate of the diol:



The diol is also of potential interest as a new raw material for the manufacture of polyester plasticisers and alkyd resins.

2,2,4 - Trimethyl - 1,3 - pentanediol, a solid, is suggested for use in synthetic lubricants and the manufacture of esters. The latter should have unusual properties in view of the configuration of the parent diol:



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(*To be continued*)

I.C.I. Spend £10 million to Make Three New Metals

TITANIUM AND ZIRCONIUM FOR CHEMICAL PLANT

THREE new metals possessing outstanding corrosion resistance, strength and nuclear properties are being made by I.C.I. at their Metals Division, Witton, Birmingham. They are titanium, zirconium and beryllium. They are very much the metals of the new age and their production requires complicated and expensive chemical and metallurgical processes. I.C.I.'s total investment in the new metals—not all of it spent at Witton—is £10 million.

The new metals project has included the commissioning of Britain's first titanium melting and fabrication plants and the country's largest zirconium plant. The latest achievement is the commissioning of the first wrought beryllium plant in Europe. The Division's research department is carrying out an extensive programme of research with these metals and with others still newer—in particular, hafnium, niobium and vanadium. Altogether, more than 600 people are engaged full-time on developing or producing new metals.

The rapid development of titanium, zirconium and beryllium has been brought about in response to the urgent demands of the aircraft and nuclear engineering industries for metals with new and ever more exacting requirements. The chemical industry is finding uses for titanium and zirconium.

All three metals possess special properties and all present the metallurgist with formidable production problems. They are difficult to extract from their ores and once the metal has been obtained it cannot be melted and turned into massive form by normal methods. Melting has to be carried out by remote control and in a vacuum.

Britain's first titanium melting plant was commissioned at Witton in 1955. It drew its raw material from I.C.I.'s General Chemicals Division, who had developed a new process, the "sodium route," for extracting titanium. Since then the pace of development at Witton has been spectacular. The latest giant furnaces can make ingots of up to 4,200 lb., compared with the original ingots of only 400 lb. The new plant has a capacity of 2,000 tons a year. Most of the titanium produced there goes to the aircraft industry. Today I.C.I.'s titanium is used in almost all Britain's most famous aircraft, including the Britannia, Comet 4 and the Argosy.

Titanium melting plant. Loading a 2,100 lb. titanium consumable electrode into a crucible prior to melting

The plant at Witton to make zirconium, used in nuclear power stations, came into production in 1958. Although zirconium is basically as difficult to produce as titanium it was launched with far fewer teething troubles because of experience already gained with vacuum melting techniques. Today the Witton plant normally produces ingots weighing half a ton but, when required, ingots weighing as much as three tons can be produced.

The beryllium plant has just been commissioned. It exists to supply the needs of the United Kingdom Atomic Energy Authority, who will use beryllium for fuel cans in their experimental Advanced Gas-cooled Reactor programme. With beryllium an extra production difficulty arises. Powdered beryllium could affect the lungs if inhaled in excessive amounts, and so special precautions have to be taken in the new plant to ensure that workers are not exposed to this risk at any stage of the process.

Titanium

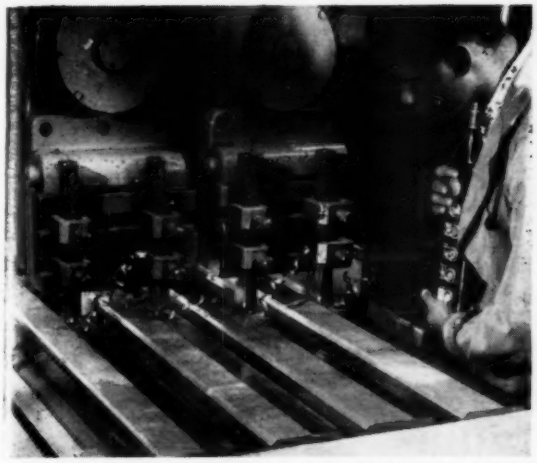
The demand for wrought titanium sprang from the need of the aircraft industry for a light metal to withstand the strains imposed by ultra high-speed flight. Titanium has a high strength/weight ratio, which is retained at higher temperatures than is considered safe for aluminium alloys, and is less affected by fatigue than most non-ferrous metals. In aircraft titanium is used among other things for fire-proof bulkheads, exhaust shrouds, compressor blades, discs, casing and bypass ducts, engine rings, forgings and bolts.

Titanium's excellent resistance to corrosion and erosion opens up an enormous range of uses. In the chemical industry it is used for complete components, for lining vessels, and for a variety of specialised applications in electrochemical processes. In nuclear reactors, titanium's short half-life makes it suitable for such components as handling gear and control rod sheaths.

In a different field again, titanium, being immune to attack by body fluids, is now replacing some of the stainless steels or cobalt alloys used for surgical implants.

Zirconium

Zirconium was the first new structural metal to be developed on a commercial scale specifically for nuclear engineering. It has three distinguishing properties: it is one of the very few metals which, when used in a nuclear reactor, absorb comparatively few neutrons; it has a good mechanical strength at moderately elevated temperatures and is compatible with uranium fuel up to a high temperature. Its chemical and physical properties are very similar to those of titanium but, having a higher density, it does not have the same attractive strength/weight ratio.



Left: **Light surface machining of forged titanium bars prior to rolling into rod.** *Right:* **Beryllium plant. Ingots of beryllium are reduced to chips on this swarfing lathe**

Certain zirconium alloys have outstanding resistance to corrosion by water and steam at high temperatures and pressures. This, and very high mechanical strength, have led to their extensive use for fuel sheathing and core components in pressurised water and boiling water reactors—such as those of the United States submarine, *Nautilus*. Britain's nuclear powered submarines will use an I.C.I. alloy, Zirconium 20, for fuel sheathing and structural components, Other zirconium alloys have been developed to suit conditions in gas-cooled and sodium-cooled reactors.

There are few uses outside the nuclear engineering field, but zirconium's high corrosion-resistance makes it important for a number of specialised purposes, particularly in chemical plant. A new use is for photographic flash bulbs. Bulbs filled with zirconium foil or fine gauge wire give a brighter flash than orthodox types and are particularly suitable for indoor colour photography.

Beryllium

Beryllium possesses extremely valuable properties which can improve the efficiency of gas-cooled reactors, thereby lowering the cost of producing power. In current gas-cooled reactors special magnesium alloys are used for fuel cans. If the efficiency of the reactor is to be raised it must operate at much higher temperatures—perhaps up to 600°C. as against the 450°-470°C. of current reactors. Magnesium alloys are not suitable for these higher temperatures, so the U.K.A.E.A. specified beryllium for its Experimental Advanced Gas-cooled Reactor, since beryllium has all the useful properties of magnesium alloys and also retains them at much higher temperatures. I.C.I. Metals Division was entrusted with the task of producing wrought beryllium for the fuel cans.

Powdered beryllium can affect the lungs if inhaled in excessive amounts so special precautions must be taken to ensure that workers are not exposed to this risk. This means that dust must be strictly controlled. The level of atmospheric contamination tolerated at the Witton plant is 2 microgram per cu. metre, equivalent in volume to half a grain of sugar in an average living room. The level of contamination in air extracted from the plant is many times less than the amount present in any domestic chimney.

There are no windows in the plant and all incoming air is filtered, heated and then extracted through machine enclosures and special ducts. The air in the building is changed every 3 min., about 200 tons of air being moved every hour. All the air is filtered before being discharged from a chimney 150 ft. high.

At every stage of processing special safeguards minimise the chance of operators coming into contact with beryllium powder and, equally essential, the quality of the beryllium being affected by contamination. Everybody in the building is supplied with a set of clean clothing for each shift and must take a shower on leaving the " contact " area. Every week 3,000 air samples are taken, both inside and outside the plant. These are analysed to ensure that the strictest standards are maintained and that there is no possible hazard to plant operators or to the general public.

In the past small quantities of beryllium have been used in X-Ray windows, but the main outlet has been for reflectors in atomic reactors. The experimental Advanced Gas-cooled Reactor being built by U.K.A.E.A. will use beryllium not only for the fuel cans but also for ancillary reactor equipment.

In other fields beryllium is interesting to aircraft engineers because of its low density and high elastic modulus. It has probably already been used in the U.S.A. for components in high-speed aircraft, guided missiles and guidance systems. There are, however, many technical and economic obstacles. The elaborate techniques required make beryllium an expensive metal. Raw beryllium costs £20 a lb. but the present quoted world price for wrought metal is about £160 per lb. Future development depends on reduced price, which in turn will be made possible by increasing demand and technological improvements.

Pharmaceutical news. The latest issue of this news sheet from Stafford Allen and Sons carries notes on quality control, syrup of raspberry, the firm's service to wholesalers and a short market report. There is also a calendar of drug crops.

PLANT AND EQUIPMENT

▶PORTABLE MIXER

The Pioneer Mixer, just introduced by Premier Colloid Mills Ltd., is described as a completely portable unit capable of mixing batches from 25 gal. to 1,000 gal. usually only possible with permanent installations.

Although the mixer can be supplied on a mobile stand, it is also suitable for clamp mounting, which gives universal movement so the mixer head can be correctly positioned in the mix.

The mixer has been designed for use at either high, medium or low speeds. Totally enclosed and flame proof, there are various motors available both for single and three phase, from ½ h.p. to 1 h.p. ranging from 400 to 3,000 r.p.m. The built-in " reduction " gearbox for the slow speed unit is integral with the motor casing, and is so small that it makes little difference to the weight or overall dimensions as compared with the directly driven unit. This novel design also ensures that the motor and mixer shaft are co-axial. The gearbox, which runs silently, is fitted with non-metallic gears, obviating the need for an oil bath, and requires only very occasional maintenance. Dependent on speed, this mixer can be supplied with a patented Dispersator or stainless steel marine-type propellers to match the particular speed and horsepower of the unit recommended. Shafts in 18/8 stainless steel come in various lengths according to requirements and can be rapidly changed from one length to another.

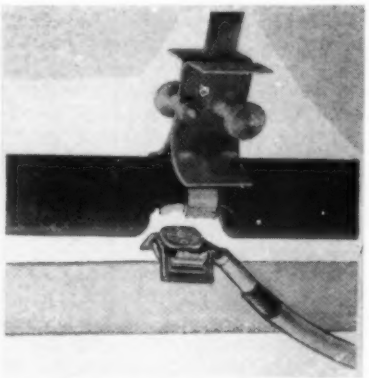
▶PIPE THERMOCOUPLES

Pipe thermocouples introduced by Cambridge Instrument Co. are designed for checking temperatures of piping of a wide variety of diameters. They are inexpensive and can be used for either short duration temperature tests in industrial plants, or for permanent temperature indicating systems in office blocks, hospitals, etc.

In tests of short duration they are normally used in conjunction with a portable indicator supplying a valuable aid to heating and ventilation engineers and inspectors.

For permanent use in buildings a number of pipe thermocouples are attached to pipe heating systems at intervals on different floors or in different rooms, and joined to a Cambridge multipoint indicator. The advantage of using pipe couples in this way is that a direct reading from the actual heating source of each room can be obtained.

Pioneer mixer, a portable unit capable of mixing batches from 25 to 1,000 gal.



Exploded view of a Cambridge pipe thermocouple fastened to one of the pipes of an ordinary flow and return heating system.

The pipe thermocouple is suitable for measuring temperatures up to 300°C. (600°F.).

In attaching the thermocouple a stainless steel ribbon is threaded through the metal eyelets forming part of the couple head, brought round the pipe, and securely fastened by means of thumb screws. The thermocouple element is thus held firmly spring-loaded against the pipe face for the required length of time. In permanent installations the steel ribbon is trimmed flush with the face of the brass holder.

▶NITROGEN PURIFICATION PLANT

Among the Birlec exhibits at the Physical Society Exhibition will be an animated flow diagram of a new type of nitrogen purification plant for the provision of super purity nitrogen. The diagram shows how commercial nitrogen from any source can be purified to meet the stringent requirements of new processes in the electrical, metallurgical and other industries which require considerable quantities of exceedingly pure nitrogen. The design concerned belongs to the group of plants developed by Birlec to provide nitrogen and other industrial gases in the grades of purity required at economic prices.

In the nitrogen purification plant compressed commercial nitrogen, containing free oxygen, is passed over a bed of heated activated copper which removes the oxygen as copper oxide, the residual oxygen content being in the region of 10-20 p.p.m. At the same time traces of carbon monoxide and hydrogen are removed. At suitable intervals the activated copper mass is reduced with hydrogen and re-used. To remove the majority of the carbon dioxide and water vapour present the nitrogen is passed, after cooling, through a vessel containing sodium hydroxide pellets.

The plant design provides further reduction in the water vapour content to a dewpoint of −80°C. by a molecular sieve adsorption unit. A Birlec molecular sieve dryer will be exhibited on the stand. Removal of the remaining traces of oxygen, carbon dioxide and water vapour takes place in a reactor containing heated gettering material.

Safety guard, with lid, developed by I.C.I. for protecting sulphur dioxide siphons.

The complete process reduces the quantity of oxygen-containing constituents in the product nitrogen to the region of 10 p.p.m.

Birlec is now known as A.E.I.-Birlec Ltd.

▶ACID COOLERS IN GLASS

In announcing a new range of sulphuric acid cooling plant, QVF Ltd. point out that, traditionally, coolers for this purpose have been constructed in lead or cast iron. The new cooler is of the serpentine type in borosilicate glass.

From the point of view of resistance to chemical attack, borosilicate glass has advantages over comparable materials. It is resistant to attack by sulphuric acid in all concentrations and at all temperatures, either under oxidising or reducing conditions. It is also resistant to mixtures of sulphuric acid with oxides of nitrogen which are common in many industrial processes. Unlike lead and cast iron, it is not vulnerable to attack by cooling water, with consequent formation of heat-insulating rust and scale.

As with other types of chemical plant, the making and maintenance of leak-tight joints on acid coolers is of primary importance. Leakage, apart from the loss of acid involved, leads to progressive corrosion of the cooler structures and of cooling water pipe lines and fittings and, where nitrous vitriol is handled, can create serious hazards to plant workers. The provision of satisfactory pipe joints in glass acid coolers—particularly those of the serpentine type—has previously offered some difficulties, due mainly to the effects of differential thermal expansion and the high density of the acid. QVF Ltd., in their new range of sulphuric acid cooling plant, have overcome this jointing problem by using an entirely new type of pipe coupling, invented and developed by Scottish Agricultural Industries Ltd. The subject of British and foreign patent applications, the coupling consists of a moulded rubber sleeve designed to fit over the tapered buttress ends of glass pipe sections and bends. The sleeve is backed by a stainless steel gaiter having lugs formed on its edges, some facing outwards and some inwards. The gaiter is secured by two worm-drive clips which are prevented from moving down the taper by the outward turned lugs, and the rubber sleeve is retained under the gaiter by the inward facing lugs. The bore of the sleeve has an insert of a special material resistant to the chemical and temperature conditions involved, and which forms a seal around the periphery of the pipe ends.

Main advantages in glass acid cooler design and construction offered by the joint include flexibility, avoidance of mechanical stress on the glass buttress ends and complete freedom from leakage. The new joint is more compact than the standard flange and allows closer pitching of cooler tubes with consequent improvement in water distribution and thermal performance.

▶GUARDS FOR SO_2 SIPHONS

Guards to protect siphons of liquefied sulphur dioxide from mishap are an obvious necessity. A recent change in the way siphons are supplied has, however, meant a revised method of guarding them.

The supplier now encloses the siphon in a cylindrical cardboard container fitted with a metal top and bottom and filled with sawdust. The container gives a measure of protection and is not meant to be removed.

A guard which has been devised by I.C.I.'s Akers Research Laboratories at Welwyn, Herts, gives a desirable extra degree of protection for these siphons. Even if the siphon container is damaged or softened by careless treatment it can still be placed inside the guard, which acts as a convenient means of carrying the siphon.

The guard stands 12 in. high and is made from 20-gauge perforated, mild-steel sheet, 16-gauge mild-steel sheet and $\frac{1}{8}$ in. mild-steel rod. The inside of the base is covered with $\frac{1}{8}$ in. rubber sheet.

For more information about the plant and equipment described please use the coupon on page 48

New plastic films. A series of booklets from British Cellophane Ltd. gives first details about the properties and uses of five new plastic films now supplied by the company. The booklets: "BCL nylon film," "BCL polypropylene film," "BCL plasticised PVC film," "BCL PVA film" and "'Styrafoil' polystyrene film" are available free of charge on application to British Cellophane Ltd., London, W.1.

Flavours and perfumes. The new, enlarged catalogue from Magnus, Mabee and Reynard, Inc. lists over 1,150 selected flavours and fragrances. It is one of the most comprehensive and practical books of its kind ever published by a member of the essential oil industry.

NEWS . . .

Fisons Group reorganised

The trading operations of the Fison Group are now being conducted through the medium of subsidiary companies. The changes took effect on January 1.

The agricultural fertiliser business is transferred to a subsidiary company, Fisons Fertilisers Ltd. The horticultural department becomes Fisons Horticulture Ltd., a subsidiary of Fisons Fertilisers Ltd.

This will involve an important change in organisation. Hitherto the board of Fisons Ltd. has been to a large extent the operating as well as the policy making organ of the Group. Now that all operating and trading activities have been transferred to subsidiaries, the executive functions of the parent board will be exercised through two managing directors, Mr. J. W. Napier and Mr. A. Wormald.

The board of Fisons Ltd., now a holding company, continues as before except that, as already announced, Mr. C. E. Horton, C.B.E., becomes a vice-chairman and Sir Ian Jacob, K.B.E., C.B., formerly Director-General of the B.B.C., joins the board.

Fisons Fertilisers, with assets of £27 million, takes over all the manufacturing and trading activities of the fertiliser division at home and overseas. The company will be the biggest manufacturer of chemical fertilisers in the U.K., providing approximately 40% of all compound fertilisers used by British agriculture. The chairman and managing director of this company will be Mr. J. W. Napier and deputy managing director, Mr. G. V. K. Burton. Other directors will be Mr. H. G. Rope, Mr. A. Gillies, Sir Anthony Hurd, M.P., Mr. E. R. Milner-Moore and Dr. J. A. Storrow.

Fisons Horticulture Ltd. will have assets exceeding £1 million. It will be responsible for the manufacture and sale of fertilisers, weedkillers and insecticides to commercial growers and amateur gardeners in the U.K. The chairman of the new company will be Mr. G. V. K. Burton, a director of Fisons Ltd., and the general manager, Mr. F. J. Heath. Other directors will be Dr. J. G. Hunter, Mr. P. M. A. Packard and Mr. K. J. S. Vasey.

The policy of Fisons Horticulture Ltd. will be to develop, through research, new products which will provide substantial advantages to the user. For the commercial grower, products possessing improvements such as their new Tip Top Fruit Fertiliser are foreseen, whilst for the amateur gardener it is intended to introduce not only new gardening products but labour-saving devices for their easy application.

Liquinure Sales Ltd., in operation since October, will be a wholly-owned subsidiary of the new company, whose interests will be extended to the Benelux countries by the formation of Asef-Fison N.V. which will be an associate company operating from Utrecht, Holland.

I.C.I. plan more and cheaper solvents

I.C.I. is to build a major extension to its trichloroethylene and perchloroethylene plants at Castner-Kellner Works, Runcorn, at a cost of £1 million.

Technical service and development work on the uses of these two solvents has been carried out by I.C.I. over many years, and this has led to a growing demand for both products, particularly in the engineering industry for metal-degreasing and also for dry-cleaning.

The extension now planned will increase the company's combined capacity for these two solvents by 25%, and will enable I.C.I. to satisfy the demands of the home market for several years ahead and permit a further increase in its present considerable export trade.

The extension will be based on a new manufacturing process which is expected to lead to lower production costs. It will be completed in 1961. Initial reductions of £1 10s. per ton in the price of trichloroethylene and £5 per ton in the price of perchloroethylene were introduced on January 1.

Cheaper polythene

The prices of *Alkathene* (I.C.I. polythene) and its compounds were reduced by 3d. a lb. for the United Kingdom market on December 22. The standard U.K. price has fallen steadily from 4s. 3d. a lb. in 1951 to 2s. 3½d. a lb. today.

Spectroscopic analysis

A course of eight lectures on spectroscopic methods of pharmaceutical analysis will be given from February 9 to March 29 at the Brighton Technical College, School of Pharmacy. Applications are now being accepted. Fee is £1.

British chemicals sell well in the U.S.

British chemical manufacturers are increasing their sales in the United States. In the first 10 months of 1959 they sold 28 million dollars' worth of chemicals to American buyers, 47% more than in the same period in 1958. The Americans are buying four categories of British chemicals: chemical elements and compounds; mineral tar and crude chemicals; drugs, perfumery and toilet goods; and plastics.

Chemical and Engineering News thinks that British manufacturers could build a big market in the U.S. to compensate for the decline in sales in the European Common Market and in under-developed countries which are now moving towards self-sufficiency in chemicals formerly bought from Britain.

Proprietary Perfumes Ltd.

Unilever's central perfumery department now operates as a company under the name of Proprietary Perfumes Ltd., with registered office at 117-121, Grange Road, London, S.E.1. The change took effect on January 1.

The directors are Mr. A. E. Diamond (chairman), Dr. R. Favre, technical director (Perfumery), Mr. D. Holness, technical director (Research), Mr. A. D. C. Lambert, commercial director and secretary.

New production facilities for John Dore

John Dore and Co. Ltd. have taken over additional premises in East London in order to increase production and offer better delivery to their clients. This factory is off High Road, Plaistow, adjacent to the East London dock area and well placed for road and rail transport.

For the time being, facilities are available for building plant units up to 5 tons in weight and up to 30 ft. high, but considerable extensions are projected for the latter half of 1960, which will accommodate plant up to about 10 tons and 45 ft. high, with a much larger factory area. During the period of temporary facilities larger plant can, however, be accommodated under outdoor gantries.

This Plaistow factory will specialise in the fabrication of chemical and allied plant in stainless and other steels and ferrous alloys. The existing John Dore works at Bromley High Street, East London will now, therefore, have more room to expand the company's well-known copper and non-ferrous manufacturing facilities.

John Dore and Co. Ltd. will thus be able to offer an even better service in the supply of plant to such industries as food, chemicals, pharmaceuticals, perfumery, soap, brewing, distillation, etc. All enquiries should be sent to the head office, at 30-34, Bromley High Street, Bow, London, E.3. ADVance 2136/7.

Antibiotics and minerals in feedingstuffs

New mixing system at Bibby's N. Ireland factory

An unusual feature of a new feedingstuffs factory being built by J. Bibby and Sons Ltd., at Lisburn, near Belfast, is that equipment will be installed for introducing minerals or antibiotics at a rate as low as 2 oz. per ton.

This exceptionally high degree of accuracy results from the development of a new system of mixing and weighing, only recently perfected by Bibby's own engineers. Thirty-two automatic feeder-weighers will feed the different ingredients into one mixing conveyor and the whole process will be controlled from an electronic panel.

Lorries bringing raw material (grain and protein cakes) into the factory will have their loads checked on a weighbridge, one of the largest ever installed in this country and able to take loads of up to 30 tons. They will then discharge into a hopper and the raw material will pass through a series of conveyors, elevators, magnets and other screening equipment to get rid of dust and other impurities.

After this the grain will be stored in 32 silos and drawn off as required. It will then pass through an automatic weighing process where minerals and additives will be introduced.

After mixing, the materials will be ground to the required fineness and passed to various machines to be made into cubes, pellets, crumbles or meal.

When the new factory goes into production early this year it will produce about 80 different kinds of animal feeding stuffs. The plant will be one of the most up-to-date in Britain and the building contractors, Holland and Hannen and Cubitts (North West) Ltd. report that their work is now in its final stages.

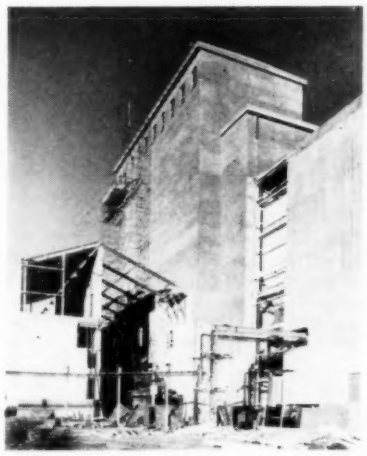
The new mill will be the sixth opened by Bibby's and the second to be built by Cubitts, who have recruited 96% of their labour force locally. It stands on a 13-acre site at Knockmore, costs about £1 million and is designed to meet the increasing demands for Bibby's products from Ireland farmers.

The firm has been supplying animal foodstuffs to Ulster for the past 60 years. Up to now products have come from the Liverpool mill, but greater demands, increased freight charges and other changes have necessitated erecting a mill on the spot.

Bibby's are the only firm supplying direct to Ulster farmers from their own transport fleet and the new mill will include a coarse dairy meal plant specially installed to meet local needs.

Cubitts have now handed over the works offices, a production and despatch block, services building electricity sub-station, compressor house, grinder house and minerals preparation building. They are now completing the remaining buildings, which comprise the administration block, boiler house and special treatment building. Most of the roadways have been completed.

There is plenty of room left on the site for future expansion as the present buildings only occupy about 5 acres.



This new animal feedingstuffs factory at Lisburn, Ireland, is being built for J. Bibby and Sons Ltd. Nearing completion in this view are the mineral building, proportioning bins and grinding house.

"M.C." article for European conference

Dr. D. B. Powell's article on the radiation sterilisation of pharmaceuticals which appeared in MANUFACTURING CHEMIST, November, 1959 (435-437) is to be brought to the attention of the Pharmaceutical sub-committee of the Western European Union by the Ministry of Health. The sub-committee will discuss the pharmaceutical uses of ionising radiations at its January meeting. The Editor of MANUFACTURING CHEMIST has granted permission for the limited reproduction of Dr. Powell's paper for circulation to the sub-committee. It had been hoped that the report on radiation of the A.B.P.I. and the Atomic Energy Research Establishment would be available for the sub-committee's meeting but it is understood that it will not be published in time.

In his article Dr. Powell discusses the technical, medical and economic aspects of radiation sterilisation. He works at the A.E.R.E.'s Wantage Radiation Laboratory.

New solvents plant

Equipment for the production of special solvents used in the manufacture of paint and lacquers, and also in the essential oils, fatty oils and rubber industries, is being constructed at BP's Kent refinery on the Isle of Grain.

This will be the first installation constructed by BP in the United Kingdom for manufacturing these products, which are known as special boiling-point solvents. It will have a capacity of 30,000 tons a year. The project consists of an acid washery and a redistillation unit as well as associated tankage, lines, pumps and loading facilities for road and rail transport.

The plant has been designed by BP, and the project is scheduled for completion this year.

Pharmaceutical conference topics

"Pharmacy and Public Relations" and "Change to the Metric System in Pharmaceutical Practice" are the two subjects to be discussed at the professional sessions of the British Pharmaceutical Conference in Newcastle-on-Tyne next September.

Congo pyrethrum agreement

Agreement has been reached in London between Mitchell Cotts Group and M. L. Hamburger for the erection of a new pyrethrum extraction plant at Goma in the Belgian Congo. A new company is to be formed in which both parties will be interested, to take over the land which has already been acquired and to erect and operate the new factory. Orders for the necessary plant and equipment have been placed, and it is anticipated that full production will be achieved with very little delay.

Congo growers will be offered advantageous prices for their flowers through the APLY organisation which already exists as a Planters Association.

The Mitchell Cotts Group technical team will ensure a consistently high quality extract of the standard produced by the Nairobi factory by seconding staff with long experience in the industry to the new venture.

Pentachlorophenol standard

British Standard for Pentachlorophenol (B.S. 3175 : 1959). Based on a draft specification of the Ministry of Defence, this new publication specifies requirements for the form, purity, crystallising point, matter insoluble in sodium hydroxide solution and total acidity of technical grade pentachlorophenol.

The material specified is used for imparting resistance to microbiological attack to materials such as wood and textiles. Appendices to the 9-page Standard deal with the determination of crystallising point, matter insoluble in sodium hydroxide solution and total acidity.

Copies of this Standard may be obtained from the British Standards Institution, 2, Park Street, London, W.1. Price 3s.

Research results and capital expenditure

Wellcome chairman is satisfied with rate of progress

Mr. Michael Perrin, chairman of the Wellcome Foundation, told members of the Wellcome Trust, who are the sole shareholders, that 1959 had been a record year. He was speaking at the A.G.M. in London last month.

Referring to the £2 million capital expenditure at Beckenham research laboratories and at the veterinary research station at Frant, Mr. Perrin said that research results had kept pace with this expenditure. He continued, " The most important breakthrough from the medical point of view was *Darenthin*, which gives an entirely new method of approach to the problems of hypertension. *Darenthin* was announced to the medical profession in July and had dominated the activities of the Therapeutic Research Division at Beckenham. The synthesis of this new drug, the discovery of its activity and the first recognition of its clinical significance had all come directly from the staff in the Wellcome Research Laboratories.

During the year several important developments had made possible the introduction of new and improved Burroughs Wellcome products in the veterinary field as well as in the medical. Chief among the former were new veterinary biological products, *Epivax-plus* and *Faunolen*, while the compound bephenium, one form of which is marketed under the name ' Frantin,' had proved itself as the most effective control yet known for nematodirus infestation in sheep. Another form of this compound was of wider significance in the medical field since, after extensive trials, it had been shown to be a most effective remedy for hookworm, from which an estimated 450 millions of the world's inhabitants are suffering. This product is being sold under the name ' Alcopar.'

Production and Sales Records. The company's production facilities had been able satisfactorily to cope with the increased range of products. Within six months of ' Darenthin ' becoming available from the research department, it was being synthesised at Dartford at a rate adequate to meet the demand which the very favourable results of clinical trials would create, thanks to some rapid and effective improvisation, while new plant was being delivered and installed. The output of biological products at Beckenham, including *Polimylex*, reached a new high level with a value three times that of five years ago.

Sales had also reached a new record at home and in direct export from the United Kingdom, as well as in the total for the 12 associated companies and branches of The Foundation overseas.

Prices and N.H.S. Prices of The Foundation's products in the United Kingdom will continue to be affected by those that can be obtained in the export market, as a result of the voluntary price regulation scheme which was negotiated with the Ministry of Health in 1957. This will come up for renewal in the near future. Despite the continuing criticism of the rising cost of the ' drug bill ' in the National Health Service, there have been indications in Parliament and the Press of recognition that the rise is more apparent than real if the fall in value of money is taken into account and if it is related to the other savings in the Health Service, which follow from the use of new and more effective drugs to prevent, as well as to cure, disease. It has been encouraging that the report of the Hinchliffe Committee to the Ministry of Health took a more realistic view of the problems which face the pharmaceutical industry, and in particular, of those related to the annual cost and the long-term financing of research."

Aromatic compounds and the Free Trade Area

At the annual general meeting of the British Aromatic Compound Manufacturers' Association the chairman, Mr. S. R. Mansfield, referred to the negotiations for a European Free Trade Area and to the subsequent proposals for a Free Trade Association among the " outer seven " countries. A joint committee set up to consider the definition of origin of Free Trade Area goods had found it virtually impossible to draw up suitable definitions by reference to process criteria but agreed that the alternative 50% value criterion would appear to be acceptable provided approval was given to the suggested list of basic raw materials to be regarded automatically as of Free Trade Area origin. This basic list comprises all the materials likely to be used by the aromatic compound industry.

The enquiry instituted jointly by the British Association for the Advancement of Science and the Association of British Chambers of Commerce about the use of the metric system had been referred to members earlier in the year. On the basis of members' views the executive committee formulated a reply which was in general favourable to the metric system of weights and measures and decimal coinage being adopted in this country. It was understood that the British Association and the A.B.C.C. would be publishing a report in February 1960.

Encouraging developments in the past 12 months had been the liberalisation measures introduced by France and Spain. As regards Spain in particular, exports had been exceedingly difficult for many years but it could now be hoped that the new facilities would enable members to enter that market on a competitive basis.

The Association had been asked to advise the Scottish Home Department about the possibilities of developing the production of natural essential oils in the Highlands but felt that such a project could not be recommended as a commercial proposition.

Jeyes—Dixon link-up

A long-term contract has been entered into between Peter Dixon and Son Ltd. (which is a wholly owned subsidiary company of Peter Dixon and Son (Holdings) Ltd.) and Jeyes' Sanitary Compounds Company Ltd. for paper supplies.

Dixons will appoint one of their directors to serve on the Board of Jeyes—Ibco Sales Ltd., and Jeyes will appoint a director to serve on the board of Bronco Ltd. (which is a wholly owned subsidiary of Peter Dixon and Son (Holdings) Ltd.).

Jeyes' Sanitary Compounds Co. will subscribe for 41,000 £1 Ordinary shares in Peter Dixon and Son (Holdings), and the latter company will subscribe for 68,000 5s. Ordinary shares in Jeyes.

Powell Duffryn buy Pipeweld Ltd.

Powell Duffryn Engineering Co. Ltd. has acquired the whole of the share capital of Pipeweld Ltd., which operates from Paston Road, Wythenshawe, Manchester, 22.

Pipeweld undertakes all forms of pipework including installations at oil refineries and at oil, chemical and gas plants as well as long distance pipelines, jacketed and terminal pipework and jetty pipework.

Refinery laboratory opened

The new laboratory at B.P.'s Llandarcy Refinery in South Wales was officially opened on December 8 by Dr. S. F. Birch, Research Associate of B.P.'s Petroleum Chemicals Department in London.

The laboratory has cost £382,000 to build and equip and has a staff of 120, which includes chemists, chemical engineers, analysts and technicians. It has facilities both for the routine testing of products made in the refinery, and for the investigation of problems associated with refining processes. In addition to a number of laboratories, the building includes offices, a conference room, library, sample store, engine test house, workshop and a reference fuels room.

Dr. S. F. Birch, who joined B.P. in 1921, discovered the sulphuric acid alkylation process in 1936 and the use of superfractionation in 100-octane aviation fuel production in 1941. More recently his interests have included the conversion of petroleum to chemicals.

People

Dr. W. A. Johnson has been appointed a director of Pure Chemicals Ltd.

The secretary and registrar of the Pharmaceutical Society, **F. W. Adams,** recently spent three weeks in West Africa. He represented the Society at the opening of the new pharmaceutical department at the Nigerian College of Technology, Ibadan, and then visited Ghana at the invitation of the Pharmaceutical Society of Ghana to assist that body in discussions with the Government on proposed new pharmaceutical legislation.

International Flavors and Fragrances Inc. have appointed **F. H. P. Trip** a vice president. Mr. Trip is now deputy managing director of the European Area Management of International Flavors and Fragrances Inc. He started his career as assistant to the management of Polak and Schwarz's Essencefabrieken N.V. In 1957 he was appointed head of the flavour division of Polak and Schwarz.

In 1958 he took an active part in the negotiations which led to the merger of Van Ameringen-Haebler, New York, and Polak and Schwarz, and in the newly formed company, International Flavors and Fragrances Inc., he became a member of the European Area Management, which covers all IFP interests apart from those in North and South America.

Fisons Ltd. announce that in view of the importance which is attached to research the Board has elected **C. E. Horton,** C.B.E., M.A., to be a vice-chairman of the company. Mr. Horton has been research director of Fisons since 1951. From 1943-45 he was Assistant Director of Scientific Research at the Admiralty and was later appointed Director of Physical Research.

Sir Owen Wansbrough-Jones has been appointed a director of The British Oxygen Co. Ltd. He is also a director of Albright and Wilson Ltd., and until last year was Chief Scientist, Ministry of Supply.

The Wellcome Foundation Ltd. have appointed **R. C. de B. Devereux** as chief engineer. Born on December 10, 1928, Mr. Devereux was educated at Repton School and at Emmanuel College, Cambridge, from which he graduated B.A. in 1952 with Honours in the Mechanical Sciences Tripos, Part I, and the Law Tripos, Part II. In the same year he joined Heinz Ltd., and in 1953 transferred to the Wellcome Foundation as engineer to the pharmaceutical division at Dartford. He became an M.A. in 1955, and in 1958 was appointed assistant engineer to the late Mr. R. L. Kennedy, a short time before the latter's premature death. Mr. Devereux is a member of the Institute of Mechanical Engineers.

R. Devereux

F. H. P. Trip

H. H. Richardson has left Shell Chemical Co. after a long period of service to take up another appointment. Mr. Richardson, who has been detergents sales manager, southern sales region since 1957, is succeeded by **D. H. Miller**, formerly commercial section head of detergents department in head office. Mr. Miller's old post is taken over by **N. Goodwin,** previously detergents sales representative in Midland sales region.

Dr. William S. Gump, research associate of the Givaudan Corporation and its subsidiary, Sindar Corporation, has received the 1959 Medal Award of the U.S. Society of Cosmetic Chemists for his outstanding contributions to the art and science of cosmetics, which included the development of hexachlorophene.

H. J. Amsterdam is the president of the U.S. Society of Cosmetic Chemists for 1960. **Dr. Sophie L. Plechner** is president-elect and will take office in 1961.

QVF Ltd. have appointed **Wolfgang Mey** as general manager of their German subsidiary company, QVF Glastechnik, Wiesbaden.

Robert E. Felton of the Felton Chemical Co. Inc. will be visiting Britain soon. He is expected to arrive on January 24 and to stay for about a month.

He can be contacted at the office of the London branch, The Felton Co. (Great Britain) Ltd., Audrey House, Ely Place, London, E.C.1.

Board change

The Board of The Chemical and Insulating Co. Ltd. has been reconstituted as follows: Mr. D. J. Grant (*chairman*); Mr. F. R. Gibson (*managing director*); Mr. G. Banks; Mr. K. C. Plumbe and Mr. F. Sawdon.

OBITUARY

Mr. Wilfrid Hill, founder of the County Chemical Co. and the inventor of *Brylcreem* hair dressing, died recently aged 91. He disposed of his interests in this product in 1939 and it is now made by the Beecham Group. Mr. Hill began business as a chemist in Coleshill, Warwickshire, and later started to make chemical accessories for the cycle trade.

Long service rewarded

Mrs. E. Taylor recently completed 25 years' service with the Liverpool soap and disinfectant firm of W. M. Delf (Liverpool) Ltd. At a meeting of the entire staff she was presented with a gold wristlet watch and a canteen of cutlery.

The presentation was made by Mrs. W. M. Delf, wife of the managing director.

Dollar drugs quota

A quota of £200,000 c.i.f. has been established for imports of pharmaceutical preparations packed ready for retail sale from the Dollar Area in 1960. This quota supersedes the Token Import Quotas for imports of these products from Canada and U.S.A. As already announced, the Token Import Scheme has been discontinued.

Details of how traders should apply for licences, etc., have been issued by the Import Licensing Branch of the Board of Trade, 43, Marsham Street, London, S.W.1.

Drama in the courtroom

"Libel"—a drama of the Law Courts—was presented by the dramatic section of W. J. Bush and Co. Ltd. at the Cripplegate Theatre, London, E.C., during the week before Christmas. The annual presentations of these talented amateurs, inspired by the Chairman of the company, Mr. Eric Bush, are always enjoyable. "Libel" takes place entirely in a courtroom and consists of closely reasoned arguments concerning the true identity of Sir Mark Loddon. This part was taken by Mr. Bush, and he was extremely well supported by the opposing counsel, who made their conflicting points with persuasion and authority. The suspense was extremely well maintained throughout three acts, and the way in which the libelled baronet conclusively proves his identity is an effective piece of drama.

Congratulations are due to all concerned for another excellent production to add to their long list of successes.

Microchemical methods

Commencing January 9, a course of 12 lectures on micro- and semi-microchemical methods with appropriate practical work is being held on Saturdays at the Norwood Technical College. London, S.E.27, from 9.15 a.m. to 12.30 p.m.

Meetings

Institution of Chemical Engineers

January 26. "Rotating Band and Spinning Band High Vacuum Distillation." 6.30 p.m. Chemical Engineering Lecture Theatre, The Manchester College of Science and Technology, Jackson Street, Manchester.

Society of Chemical Industry

February 4. "The Soiling of Textile Materials," by T. H. Morton. 7.30 p.m. Demonstration Theatre, Gas Showrooms, Parliament Street, Nottingham.

Institution of Plant Engineers

January 26. "Safety in Uses of Industrial Gases and Equipment," by M. T. Reeks. 7.30 p.m. South Wales Engineers' Institute, Park Place, Cardiff.

January 28. "Instrumentation," by R. H. Baulk. Grand Hotel, Sheffield.

Royal Institute of Chemistry

January 29. "Opportunities in Chemistry," by J. H. Skelton and N. Booth. 6.30 p.m. Brighton Technical College.

February 4. "Water Repellent Surfaces," by N. K. Adam. 6.30 p.m. Kingston Technical College, Fassett Road.

February 8. "Reaction Mechanisms," by E. D. Hughes. 6 p.m. Sir John Cass College, Jewry Street, E.C.3.

Royal Society of Arts

February 3. "Modern Dyes," by C. Paine. 2.30 p.m. R.S.A., John Adam Street, Adelphi, W.C.2.

Society for Analytical Chemistry

January 20. "Antibiotic Assays in Body Fluids," by L. Garrod. 7 p.m. Meeting Room, Chemical Society, Burlington House, Piccadilly, W.1.

Chemical Society

January 21. "Chemistry of Pyrazoles," by I. L. Finar. 5 p.m. Edward Davies Chemical Laboratories, University College of Wales, Aberystwyth.

January 21. "Synthetic Detergent Washing Powders," by L. N. Savidge. 8 p.m. University Union, Aberdeen.

January 21. "Some Recent Studies with Natural Products," by E. R. H. Jones. 4.30 p.m. Chemistry Dept., The University, Sheffield.

January 22. "Energy Transfer in Gases," by T. L. Cottrell. 4 p.m. Chemistry Dept., The University, Glasgow.

January 25. "Some Models of Physical Adsorption," by D. H. Everett. 5.30 p.m. Chemistry Dept., University College, Cathays Park, Cardiff.

January 25. "Reactions in Liquid Dinitrogen Tetroxide," by C. C. Addison. 5 p.m. Science Laboratories, South Road, Durham.

January 26. "Electron Resonance of Free Radicals," by D. H. Whiffen. 7.45 p.m. Dept. of Chemistry, Queen's University, Belfast.

January 26. "Hydrocarbon-metal Carbonyls," by P. L. Pauson. 8 p.m. Chemistry Dpet., The University, Nottingham.

January 28. "Synthesis and Dissolution of Starch in Plants," by H. K. Porter. 5.45 p.m. Dept. of Chemistry, University College of N. Wales, Bangor.

January 29. "The Structure of Myoglobin," by J. C. Kendrew. 8.30 p.m. University Chemical Laboratory, Lensfield Road, Cambridge.

January 29. "Activation of Carbon-Carbon Double Bonds by Cationic Catalysts," by A. G. Evans. 5.30 p.m. Chemistry Dept., King's College, Newcastle upon Tyne.

January 29. "Homogeneous Catalytic Activation of Molecular Hydrogen," by J. Halpern. 5 p.m. Chemistry Dept., The University, Southampton.

February 1. "Structure and Reactions of the Gallium Halides," by N. N. Greenwood. 6.30 p.m. College of Science and Technology, Manchester.

February 2. "The Behaviour of Ionic Solutions in Hydrogen Peroxide," by W. F. K. Synne-Jones. 5 p.m. Chemistry Dept., The University, Nottingham.

February 2. "Ionic Crystals and their Melts," by A. R. J. P. Ubbelohde. 8 p.m. Chemistry Dept., The University, Sheffield.

February 3. "Some Aspects of the Chemistry of Quaternary Ammonium Compounds," by J. McKenna. 5.30 p.m. Dept. of Chemistry, University College, Dublin.

February 4. "Chemisorption on Platinum," by J. G. Aston. 5.15 p.m. Dept. of Chemistry, The University, Bristol.

February 4. "Atomic Reactions," by J. W. Linnett. 5 p.m. Organic Lecture Theatre, Chemistry Dept., The University, Hull.

February 4. "Some Recent Advances in the Synthesis of Fatty Acids and Phospholipids," by R. E. Bowman. 7.45 p.m. University Chemical Laboratory, Trinity College, Dublin.

February 5. "Big Rings," by R. A. Raphael. 4.30 p.m. Large Chemistry Lecture Theatre, The University, Birmingham.

February 5. "Some Antibiotics derived from Actinomycetes," by A. W. Johnson. 8.30 p.m. University Chemical Laboratory, Lensfield Road, Cambridge.

February 5. "The X-Ray Analysis of Molecular Structure," by D. M. Crowfoot-Hodgkin. 5 p.m. Washington Singer Laboratories, Prince of Wales Road, Exeter.

February 8. "The Anti-knock Action of Tetraethyl-lead," by A. D. Walsh. 5 p.m. Science Laboratories, South Road, Durham.

February 8. "Alkali-metal Derivatives of Organic and Organometallic Compounds," by G. E. Coates. 4.30 p.m. The University, Leicester.

February 9. "Looking for New Drugs," by F. L. Rose. 4 p.m. Large Lecture Theatre, Chemistry Department, The University, Manchester.

February 11. "Hydrocarbon-metal Carbonyls," by P. L. Pauson. 7.30 p.m. Lecture Theatre, The Royal Institution, Albemarle Street, W.1.

February 12. "Vitamin B_{12}," by A. W. Johnson. 5.15 p.m. Chemistry Dept., St. Salvators College, St. Andrews.

February 12. "Hydrocarbon-metal Carbonyls," by P. L. Pauson. 5 p.m. Lecture Theatre, Engineering Dept., The University, Southampton.

February 15. "Some Aspects of the Structural Chemistry of Platinum," by E. G. Cox. 6.30 p.m. Chemistry Lecture Theatre, The University, Leeds.

February 18. "Biogenesis of Porphyrins," by A. W. Johnson. 5.15 p.m. Dept. of Chemistry, The University, Bristol.

February 18. "Chemotherapeutic Research," by F. L. Rose. 7.30 p.m. Technical College, Brunswick Road, Gloucester.

February 18. "Some Reactions of Bicycloheptadiene," by R. C. Cookson. 4.30 p.m. Chemistry Dept., The University, Sheffield.

February 19. "Some Glimpses into the Variations which Nature brings about in Acetylenic Compounds," by N. A. Sørensen. 8 p.m. University Union, Aberdeen.

Society of Cosmetic Chemists

February 12. "The Design of Experiments," by M. H. Quenouille. 7.30 p.m. Royal Society of Arts, John Adam Street, London, W.C.2.

Distillation—International Symposium

Experts from all over Europe are expected to gather in Brighton next May for what is likely to prove a major landmark in the long history of distillation. The International Symposium on Distillation is to be held there on May 4, 5 and 6 as a meeting of the European Federation of Chemical Engineering.

The preliminary programme contains 29 papers from experts on distillation in nine countries. The Organisers (The Institution of Chemical Engineers, London, and the Chemical Engineering Group of the Society of Chemical Industry) have selected from the papers offered those which give the greatest promise of revealing original information applicable in a wide field.

Enquiries to The General Secretary, The Institution of Chemical Engineers, 16, Belgrave Square, London, S.W.1.

News from Abroad

ITALY

Ciba-Lepetit factory

Antibiotics and other fermentation products will be produced in a new pharmaceutical factory which is to be built near Naples. The joint owners will be the Soc. Lepetit of Milan and CIBA of Basle. The works is to be known as Fervet (Fermentazione del Vesuvio—Torre Annunziata).

SPAIN

Naarden subsidiary

N.V. Chemische Fabriek Naarden has established "Naarden" Productos Orgánicos S.A. in Barcelona.

The new subsidiary will operate a factory, now under construction, which will produce basic materials for the food industries. These will include bulk products such as sodium benzoate and benzoic acid.

HUNGARY

Big plans for the chemical industry

Details of the way in which Hungary's chemical industry aims to double output during the next five-year plan period (1961-65), announced last month, have been given by Dr. György Somló, Director of the National Chemical Works Planning Office, in Budapest.

He told the newspaper *Népszava* that 25 major building projects in the industry were scheduled under the plan, and these included the modernisation and reconstruction of some existing works as well as the building of several new plants.

This compared to eight such projects completed during the twelve years from 1949-60.

"We are now working on plans for the reconstruction of four pharmaceutical factories and are drafting plans for a big new factory in this field," said Dr. Somló.

"Plans for a synthetic materials processing plant at the Hungaria Synthetic Materials and Rubber Works are nearly ready, and we are working on plans for the reconstruction of the rubber factory there. We are also planning to build a new rubber factory in the provinces, as an extension of the Hungaria works."

At Borsod a new P.V.C. plant was being built, and, said Dr. Somló, it was hoped that a new factory for the manufacture of caprolactam—a raw material for synthetic yarn which has a polyamide base—will begin production under the five-year plan. Plans for the polythene plant at the Tisza Region Chemical Combine, north-east Hungary, were also being drafted.

The big increase in the production of usperphosphate (from 200,000 to 650,000 tons annually) proposed in the plan will be achieved partly by the construction of a new superphosphate factory in Szolnok, eastern Hungary.

(The new artificial fertiliser factory of the Tisza Region Chemical Combine, which will use methane gas piped from Rumania, is already under construction. It is scheduled to produce 210,000 tons of nitrogenous fertiliser annually by 1964.)

Other projects on the drawing boards of the Planning Office, said Dr. Somló, include three sulphuric acid plants, a powder dye factory and a new oil refinery at Szászhalombatta, central Hungary.

SWEDEN

New starch plant replaces 16 factories

A central starch factory replacing no less than 16 old plants has been opened at Jämshög, in the South Swedish province of Blekinge. The new factory forms part of a modernisation and concentration scheme in the Swedish starch industry carried on by the Swedish Starch Producers' Association, a farmers' co-operative. Ten years ago there were 140 starch factories in Sweden, now the number is 70. The association plans to open one new central plant annually over the next few years.

The Jämshög factory is largely automated and is operated by a staff of 12. The capacity is one ton of starch from 5 tons of potatoes per hr. The total output from September 20 to Christmas was estimated at some 2,000 tons of starch.

The disposal of the waste water from the factory—which, if let out into the waterways, would pollute them—has been solved by a system of water guns. At Jämshög 80 hectares of neighbouring fields are being fertilised in this way.

The Swedish starch industry annually uses about 125,000 tons of potatoes and produces a total of 25,000 tons of starch, all of which is consumed within the country. Most of it goes to the chemical industry, where it is used in the manufacture of such varied products as paper, textiles, cosmetics, wall-papers, cake-mix, canned soup, floor varnish and candy.

CANADA

Chemical Specialties Association

Mr. Geoffrey H. Wood, G. H. Wood and Co. Ltd., Toronto, was elected president of the Canadian Manufacturers of Chemical Specialties Association at its second national convention in Toronto. Over 200 delegates from all parts of Canada and the U.S. attended, representing companies which manufacture chemical specialties, such as disinfectants, brake fluids, soaps, detergents, aerosols, floorwaxes, etc.

SOUTH AFRICA

S.A. Druggists sell subsidiary

South African Druggists Ltd. have sold the entire assets of P. Grant Smith Ltd., one of the pharmaceutical divisions dealing in dental equipment and dental products, to the Amalgamated Dental Co. Ltd., of England, for a figure in the region of £250,000. The chairman of South African Druggists Ltd. said that the field of operation of P. Grant Smith Ltd. is in some ways outside the basic field of operation of South African Druggists Ltd., whose activities are essentially in the field of manufacture and distribution of pharmaceutical products and allied merchandise.

Pharmaceutical company changes hands

The Federale Volksbeleggings Group, which has been closely associated with the pharmaceutical trade for a number of years through its interests in Sana Ltd., has acquired the controlling interest in Petersens Ltd. The group will now become more active in the pharmaceutical and photographic trade. Petersens, established in 1842, is one of the oldest concerns in the South African pharmaceutical trade. It has a modern factory in Cape Town and several valuable overseas agencies for ethical and other preparations. It also makes a variety of preparations under its own name. It has the sole agencies for South Africa and the Rhodesias for Voigtlander, Eumig and Johnson's photographic equipment. Petersens have offices and depots in all the important cities of the Union.

Polio vaccine hopes

The director of the South African Institute of Medical Research said that polio may soon be conquered. Research into polio was intensified after the first outbreak in 1948. "The Government did not see its way to contribute any additional funds for polio studies, but an appeal to the public brought a quick and generous response. Within a fairly short time £500,000 was collected, and it was possible for the Poliomyelitis Research Foundation to erect modern laboratories at Rietfontein, outside Johannesburg, to work in close association with virus laboratories in other parts of the world. At present a team of American doctors is working with our doctors at Rietfontein. The result of these studies is the production of a vaccine which, at first, was only partially effective. Now, however, we are within sight of a live virus which holds out a reasonable possibility that the disease may soon be banished permanently from the world." He said that the staff and work of the institute had increased

fourfold in the last 20 years. " Compared to several other countries, however, the grants we receive are meagre. The Union Health Department and the Council for Scientific and Industrial Research and the Chamber of Mines gives us £7,500 a year. Most of our income is derived from the moderate charges we make for preparing vaccines and sera, and for examining a million blood and other specimens annually. With more funds less highly qualified people could be employed to do routine work, letting the specialists do more research."

Attack on cosmetics

Durban's medical officer of health says Bantu teenage girls are going without food to buy powder and lipstick. This " cosmetic infatuation " is due to confusion caused partly by commercial advertising, persuasive salesmen and the Bantu's general inability to assess relative and contemporary values. He said: "Until recently the healthy brown skin of the Bantu woman was unassaulted by the powders of the parlours. Now a number of them disguise their natural complexions by layers of white powder, their lips smudged to a sickly red. This is a triumph of advertising. The money thus expended should have been used for food."

Time to expand?

Increased production of light chemicals in South Africa is likely in the future, as more domestic capital is available for industrial development than for some time past and current interest rates are relatively low. The question is thus not so much of when but how much should industry expand and improve its efficiency. Some economists consider that the country is on the threshold of a new era of prosperity.

UNITED STATES

Spray tower model for university

A plastic spray tower first used as a working model in the design of more efficient commercial soap and detergent towers has been presented to the department of chemical engineering, University of Delaware, by the Colgate-Palmolive Co.

The tower was made especially for studying air flow under various conditions and has several unique design features. Some of the towers eventually built as a result of experimentation with this model are eight storeys high and 22 ft. in diameter.

Dr. Robert L. Pigford, chairman of the department of chemical engineering, accepted the gift from Dr. R. B. Wearn of Colgate, and expressed the appreciation of the university. He said that the tower would be used in connection with a special problems course for undergraduate students studying flow theory.

Dr. R. B. Wearn *(left)*, **director of research and development for the Household Products Division of the Colgate-Palmolive Co., explains the use of a plastic spray tower to Dr. R. L. Pigford, chairman of the department of chemical engineering, University of Delaware. The tower was given to the university for experimental work in flow theory**

Colgate enters ethical drug field

The Colgate-Palmolive Co. have agreed to acquire Lakeside Laboratories, Inc. in exchange for Colgate stock. This acquisition marks Colgate's entry into the ethical drug field as announced earlier this year by Edward H. Little, chairman.

Lakeside Laboratories Inc., located in Milwaukee, was founded in 1924. Drugs produced by Lakeside are widely used by doctors and in hospitals for the treatment of heart conditions, mental depression, anæmia, asthma and gastro-intestinal disorders. These products are available to the public only on a doctor's prescription.

A major share of Lakeside's present sales is represented by ten specialty products, nine of which were developed in the company's own laboratories during the last seven years. The company's total sales in 1958 were over £6 million. Lakeside's pharmaceuticals are now being sold in 62 countries.

Upon consummation of the arrangement Lakeside will operate as a wholly-owned subsidiary of Colgate-Palmolive.

ISRAEL

Chemistry for the blind

The Jerusalem Institute for the Blind plans to open a special laboratory where its students will be able to perform experiments in chemistry and physics on a secondary school level. The laboratory will be opened if there are volunteers ready to build the instruments required for these experiments.

This new development in the education of the blind has been made possible by Abraham Wexler, an Australian Jew and a chemist, who has devoted 50 years to investigating the problems of the blind.

He has developed a number of special instruments enabling blind students to do experiments in physics and chemistry. These are designed to enable the senses of hearing and touch to do the work of sight. For example, the blind student is able to measure temperature by feeling a special wheel, which he stops when he hears the sound made when a probe touches the mercury in the tube of a thermometer.

AUSTRALIA

Shell—I.C.I. petrochemical project

An agreement involving the construction of new and expanded plant for the manufacture of petroleum chemicals in New South Wales has been reached between Shell Chemical (Australia) Pty. Ltd. and Imperial Chemical Industries of Australia and New Zealand Ltd.

Shell Chemical will erect an ethylene manufacturing and purification unit at Clyde, N.S.W., in association with Shell's refinery there. The ethylene so produced will be piped to ICIANZ at Botany, N.S.W., where its immediate use will be in the manufacture of polythene.

ICIANZ's plant at Botany, already extended several times, is currently being further increased, and the total investment represented by ICIANZ's extended facilities at Botany and Shell's new ethylene plant at Clyde will be over £A10 million. Adequate supplies of ethylene will be available to meet ICIANZ and Shell's requirements for many years to come.

The new plant at Clyde is expected to come on stream within two years. Wherever possible, locally manufactured material will be used in its construction.

New chemical industries

Discussions are now being held between the Collier Carbon Chemical Co. of the United States and the Gas and Fuel Corporation of Victoria for the founding of a £40 million chemical industry in Victoria. The latter company is also discussing the establishment of a plastics factory in conjunction with the Timbrol Co. of Rhodes, New South Wales.

Institute president

Mr. C. E. C. Nicholls, manager of C.S.R. Chemicals Pty. Ltd., Sydney, has been elected president of the Royal Australian Chemical Institute.

Pharmaceutical and toilet preparation production

There were 212 factories in Australia manufacturing pharmaceutical and toilet preparations at June 30, employees numbering 6,834 with an annual salary and wage bill of £5,531,000. Cost of raw materials used during the year was £18,226,000; power, fuel and light cost £386,000; and the total value of output was £40,468,000.

Production included:

Proprietary medicines, £21,237,910; veterinary medicines, £1,199,617; composite make-up, £511,888; cosmetic creams and lotions, £1,695,001; dentifrices, £2,761.782; deodorants, £318,848; depilatories, £58,112; hair preparations, £1,552,950; home perm kits, £556,629; face powder, £357,506; lipstick, £866,253; mascara and eye make-up, £66,099; rouge, £88,754; talcum powder, £959,310; and toilet lanoline, £32,426.

New plant for tanning extracts

Industrial Extracts Ltd., manufacturer of tanning extracts, has installed equipment for the production of a spray-dried extract at a cost of some £30,000. Directors of the company expect a ready sale for extract in powder form in preference to the solid previously produced. For the year to June 30, the company made a profit of £37,306 compared with the £37,371 of the previous 12 months. Ordinary dividend has been lifted from 7½ to 10%.

Further import easing

Australia's import licensing ceiling has been lifted by an extra £25 million to £875 million a year, and in addition discrimination against dollar goods has been further eased.

PAKISTAN

First penicillin factory

The Pakistani Government penicillin factory at Daudkhel has gone into production. During the first year the plant is estimated to produce 10 million mega units of penicillin, which will meet the entire requirements of this drug in the country.

The present annual consumption in Pakistan is about 7 million mega units and the factory was planned for approximately that capacity.

The actual annual production now estimated at about 10 million is based on the excellent yield of penicillin during the test run. The yield, which is much better than was first expected, is due to the improved strain of the fungus cultured in a suitable medium.

The penicillin plant—a project of the Ministry of Health—has been completed with the help of UNICEF, who provided the equipment, and an American firm, who loaned the services of experts.

The plant is likely to be expanded later to a yearly production capacity of about 15 million mega units.

JAMAICA

Colgate Palmolive plan £100,000 factory

Colgate Palmolive Ltd. is making plans to manufacture dental cream in Jamaica, reports Barclays Bank D.C.O. from its office in Kingston. It is expected that the new project will involve a capital expenditure of £100,000 and employ approximately 40 persons. It is proposed that the new factory will be built on the industrial estate and will go into operation in September.

NEW COMPANIES

These particulars of new companies have been extracted from the daily register of Jordan and Sons Ltd., company registration agents, Chancery Lane, London, W.C.2.

Bloomsteins Pharmacy Ltd. 10.11.59 12 Northfield Avenue, West Ealing. Pharmaceutical Chemist. £100. Dir.: D. Bloomstein.

Bradley Pharmacy Ltd. 10.11.59. 39 Brocklesby Rd., Grimsby. £10,000. Sub.: F. Hard.

Hague (Moseley) Ltd. 29.10.59. 123 Alcester Rd., Moseley, Birmingham 13. To carry on bus. of mnfrs. of and dlrs. in cosmetics and beauty preparations, etc. £1,000. Dirs.: Mrs. C. Hague and Anthony P. Hague.

Northwood Pharmacies Ltd. 30.10.59. £3,000. Perm. Dir.: H. Northwood, Jr.

Maria St. George Ltd. 30.10.59 Mnfrs. and dlrs. in cosmetic, toilet and beauty preparations, etc. £1,000. Sub.: D. St. George, 12 Phillimore Terrace, London, W.8.

Talanol Ltd. 30.10.59. Importers, exporters, manfrs. of and dlrs. in medicinal, lotions, patent medicines, etc. £100. Perm. Dir.: R. Green, 55 Oakley St., London, S.W.3.

Yamac Ltd. 30.10.59. 77 Portland Place, London, W.1. Wholesalers, mnfrs. of, dlrs. in and mchts. of chemicals and drugs, etc. £100. Dir.: L. Wiener.

Lister's Chemists Ltd. 3.11.59. 43 Upper Berkeley St., London, W.1. £100. Dirs.: Eric Lister and Samuel Hornstein.

Cray Drug Co. Ltd. 1.10.59. 248 Court Rd., Orpington, Kent. £100. Dir.: R. C. A. Broadley.

Moseley Cosmetics Ltd. 1.10.59. £100. Sub.: M. Moseley, 92 Portland Place, London, W.1.

Toxic Products Ltd. 5.10.59. 48-50 Uxbridge Rd., Ealing, London, W.5. Chemical mnfrs. and mchts. £5,000. Dir.: C. L. J. Chapman.

D. J. Paterson (Chemists) Ltd. 6.10.59. 135 Rochester Way, London, S.E.3. £1,000. Dir.: D. J. Paterson.

Mark Laboratories Ltd. 6.10.59. Experimental and consulting chemists. £2,500. Sub.: R. M. Lucas, 3 The Crescent, North Wembley, Middx.

Technical Press Review—January

Corrosion Technology.—Corrosion Research in Singapore; Research at the American National Bureau of Standards; Corrosion Symposium.

Chemical and Process Engineering.—Materials Handling in the Chemical and Allied Industries; Crystallisation; Swedish Heavy Water Process.

Automation Progress. — Magnetic Tape Units for Computers; Photocells in Perspective; British Photo-electric Transducers; Electrical Tape Control for Drill Turret and Table; Recognition and Control of Speech; A Computing Centre for Air Traffic Control.

Petroleum.—Shell Haven Chemical Fertiliser Plant; Petrochemicals at Grangemouth.

Paint Manufacture.—High Boiling Solvents for Nitrocellulose Lacquers; Functions of Paint Solvents; Silicones Improve Wax Polishes.

Food Manufacture. — Grinding and Milling Machinery; James Keiller Factory; Annual reviews—Confectionery, Pickles and Sauces; How is Flavour to be Judged.

Fibres and Plastics. — Resin Finishing of Textiles; Shrinkproofing Textiles and Polyamides; Chemical Shrinkage of Fabrics; Polypropylenes —Structure and Properties.

Dairy Engineering.—Cold Store Design; The Bacteriology of Milk Refrigeration; Refrigeration Plant and Equipment.

World Crops.—The Pattern of Seed Dressing Development; Hybrid Seed Corn in the Tropics and Sub-Tropics; Silage Maize in Northern Europe; The Cultivation of Wheat on Ridges; State of World Agriculture.

For specimen copies and subscription forms apply to the Circulation Manager, Leonard Hill House, Eden Street, London, N.W.1.

Aluminium aspirin

In a news item on p. 469 of the November issue we stated that aluminium aspirin is made by Monsanto Chemicals Ltd. In fact Monsanto did some work on the product about three years ago but did not carry it any further, and do not supply it. We apologise for our misunderstanding of a telephone conversation.

New Products

Penetration agents

A series of diffusion and penetration agents for pharmaceuticals has been marketed by Jacobson Van Den Berg and Co. (U.K.) Ltd. Called *Labrafils*, they are interesterified vegetable oils made in France by Gattefosse. Their most marked property is their power of diffusion. They are recommended as ingredients for a number of preparations, including nasal oils, parenteral oils, percutaneous fluid vehicles, injectable oils, dermatological preparations, suppositories, ovules, etc. They are claimed to be completely non-toxic and non-irritant. Prices range from 14s. 9d. to 23s. 6d. per kg. in 100 kg. lots. A booklet explaining the properties and uses of Labrafils is available from Jacobson Van Den Berg and Co.

Placental extracts

A range of human placenta and bovine embryo extracts in a variety of forms is being introduced by Jacobson Van Den Berg and Co. (U.K.) Ltd., agents for the manufacturers, Gattefosse, Lyons, France. There are three categories: Filatoy extracts (human placenta or bovine embryo); Glycero-Glycolic extracts (human placenta); Total Lyophilised extracts (human placenta or bovine embryo).

Prices range from 57s. 6d. to 245s. per litre.

Perfume modifier

Agrumenal has been introduced by Dragoco who describe it as a strong fresh and spicy speciality with a verdant note. It is of liquid consistency; light green colour; clearly soluble in mineral oil up to 2% and in ethyl alcohol of 85% by volume up to 1%. It is stable in white and coloured soaps and suitable for creams. It is recommended as a modifier of eau de cologne oils and citrus compounds. Combinations with flower oils give novel effects. It accentuates the Bergamot effect in any compound.

Two qualities are supplied — at 141s. 6d. and 52s. 6d. per lb. respectively.

Trials should be started with very small quantities, up to 1-5% on the compound. U.K. agents are Bruce Starke and Co. Ltd., London, E.C.3.

Deodorised lanolins

Under the trade name Centralin a range of highly refined lanolins and lanolin derivatives is now being produced by Pura-Lanolin Ltd. at their modern factory in Bradford, Yorkshire.

Of particular interest to the pharmaceutical industries are three high quality lanolins—superfine, extra and standard. All meet the B.P. specification, and, by a vacuum deodorising process recently developed by the company, set a new standard of virtual freedom from odour. These lanolins may be stabilised against oxidation as required.

Samples and technical data are available from the company at Gibson Street, Bradford, 3.

Shampoo ingredient

A sodium lauryl sulphate of higher purity and lower viscosity than previous types has been developed by the Du Pont Co. specifically for use in shampoos.

The product, to be marketed as *Duponol* QC surface active agent, permits making a full range of shampoo products from clear liquids to pastes. It can be used to obtain clear liquid shampoos with adequately low cloud points without the addition of alkylolamine salts. Its most noticeable property is its very low viscosity and flat temperature-viscosity curve which make it easy to handle, particularly in cold weather.

Duponol QC, an anionic surfactant, is supplied as an aqueous and slightly viscous solution containing about 30% sodium lauryl sulphate. It is soluble in water in all proportions and shows excellent foaming properties in both hard and soft water and in the presence of greasy soils.

Fungicide-germicide

Onyx Oil and Chemical Co., Jersey City 2, U.S.A., has made available a 75% concentrate of n-Alkyl (50% C_{12}, 30% C_{14}, 17% C_{16}, 3% C_{18}) isoquinolinium bromides. Called *Isothan* Q-75, this germicide-fungicide is claimed to be highly active against many representative fungi. It can be used as an ingredient of dandruff rinses and shampoos, as an agricultural fungicide and for the control of athlete's foot.

New molecular models

Units from which molecular models, accurate with respect to stereo characteristics, can be quickly built up have recently become available in this country. The units consist of little rods and tubes which are soldered together at the correct angles at a point representing the atomic nucleus; the free ends represent atoms of hydrogen so that the individual units represent CH_4, H_2O, NH_3, etc.

Stereomodels are assembled by introducing the rod of one unit into the tube of another and a push button type of mechanism holds the atoms at the correct internuclear distance (1 cm. represents 0·4Å) without hindering the free rotation of the rods in the tubes. When two or more atoms are attached to a bond which cannot be rotated under ordinary conditions, they are represented as a single unit; the two principal nuclei are soldered together at the correct distance. A simple system of marking allows easy differentiation between isolated, conjugated and aromatic double bonds and different atomic nuclei are readily distinguished at a glance by their distinctive colouring.

Büchi stereomodels have a number of advantages. Only the central axes of the bonds are shown and the omission of the electron clouds gives a very clear view of the geometrical relationships and permits easy measurement of internuclear distances. The units are constructed of stainless steel and normal use does not deform them or otherwise wear them out. Stereomodels are small enough for convenient handling and require so little room that a considerable number of units can be carried in the pocket.

The units are made by the Swiss Büchi company whose agents are L. Light and Co.

Emulsion for Space Research

Ilford Ltd. have shipped 12 cwt. of their special G.5 nuclear emulsion to the U.S. for use by Prof. Schein and his team of scientists at the University of Chicago.

It is the largest order of its kind Ilford (nearly all of this special material used throughout the western world is made by this firm) has ever supplied, and is said to be worth around £40,000.

The emulsion, flown at a height of more than 100,000 ft. in two specially-constructed gondolas measuring 7 ft. by 6 ft. by 6 ft., will record the distintegrations produced by nuclear particles of enormous energy coming from outer space.

Because of the size and weight of the loads, balloons of 10 million cubic ft. capacity will be used. They will be launched from a U.S. Navy aircraft carrier off Hawaii, in the Pacific.

The manufacture of G.5 nuclear emulsion has many problems, not the least being its storage after manufacture. Refrigerated storage under a lead cover, in the basement of Ilford's new research laboratory, guards against deterioration and reduces exposure to cosmic rays so far as is practicable.

The solid sheets of emulsion (they have no film, glass, or other "base") will be packed in 500-sheet "stacks" measuring 24 in. by 18 in. by 11½ in.; plastic foam will supply the heat insulation.

The quantity of silver involved is enough to coat a million popular-size roll films!

Packaging

6-oz. Aerosol containers

The John Dale Group are now producing, as standard, an all-aluminium two-piece 6-oz. container.

These cans are supplied with an aluminium base rolled on to an aluminium impact extruded body, and this removes any possibility of can corrosion due to bi-metallic action, rusting at the base with the consequent deposit marks on shelves and tiled surfaces and, in certain instances, the necessity for internal protective lacquerings.

Plastic roll-on bottles

Two new roll-on bottles have recently been introduced by Lacrinoid Products Ltd. These two bottles, manufactured for Yardley's *Poise* and Care Laboratories' *Check*, are moulded entirely from plastics.

The bottle itself is produced from polythene and is blow-moulded. The balls are injection-moulded from polystyrene, and the caps are compression-moulded from urea formaldehyde.

The *Poise* bottle is silk-screened in two colours, magenta and white, the materials themselves being a natural pink. The *Check* bottle and cap are bright yellow in colour, the bottle having an embossed decoration. A printed outer in red, blue and yellow surrounds the *Check* bottle.

Tablet packs restyled

Moore Medicinal Products Ltd., of Aberdeen, have restyled the packaging of *Codasphen* and *Tetride* with the co-operation of the Plastics Group of The Metal Box Co.

Codasphen will be marketed in white polystyrene Polytubes, printed in red and dark blue. Tetride will also be marketed in white polystyrene Polytubes, but the printing is dark blue and yellow, with white lettering.

Codasphen is an analgesic for the relief of headaches, neuralgia, colds, influenza and joint infections. It will retail at 1s. 11d. per tube of 12 tablets.

Tetride tablets are for the alleviation of fibrositis, lumbago, dysmenorrhœal and muscular pain. Until recently Tetride had ethical promotion to doctors only, in packs of 50 and 500 tablets. For the time being it will not be retailed overseas. Tetride will retail at 2s. 5d. per tube of 16 tablets.

T.B. cachet incorporates dosage reminder

To minimise the risks of patients forgetting their T.B. dosage schedule Smith and Nephew Pharmaceuticals have now introduced *Pycamisan* B.D.; cachets containing 1·5 g. sodium P.A.S. + 37·5 mg. isoniazid presented in polythene tubes of 8. Each tube contains one day's supply divided into two—one half marked " morning, " and the other half " evening, " designed to tell the patient exactly what his dose is and when to take it. The awkward midday dose is eliminated, yet the cachets provide a full daily dose of 12 g. P.A.S. and 300 mg. isoniazid—the most widely prescribed combination in current use. A new, small size cachet is used for the first time, and an easier method of taking the cachets has been evolved. A fully illustrated enclosure leaflet is provided, and the cachets are packed in containers of 240 and 480—1 month's and 2 months' supply respectively. The packs retail at 67s. 6d. (240 tablets) and 127s. 6d. (480).

One day's supply of T.B. cachets is packed in this polystyrene tube marked with dosage times from Smith and Nephew

★

All-aluminium, two-piece aerosol containers

★

New polythene tube packs for Moore Medicinal Products

Greetings acknowledged

We received Christmas cards from many of our friends, and in particular we would like to acknowledge the following:

Westminster Laboratories Ltd.
Helena Rubenstein
L. Givaudan and Co., Geneva
Glaxo Laboratories Ltd.
Coene Père and Fils S.A., Brussels
J. A. Baptiste d'Almelda Lda.
Dodge and Olcott Inc.
Pfizer Ltd.
Marchon Products Ltd.
Duncan, Flockhart and Co. Ltd.
E. F. Leak and Co. Ltd.
The Distillers Co. Ltd.
May and Baker Ltd.
A. Boake, Roberts and Co. Ltd.
The Wellcome Foundation Ltd.
The British Man-made Fibres Federation
Gordon and Gotch (Sellotape) Ltd.
Aplin and Barrett Ltd.
Roche Products Ltd.
Rumble Crowther and Nicholas Ltd.
The Yale and Towne Manufacturing Co.
" Naarden "—Holland
The Winter Thomas Co. Ltd.
Macfarlane Watson Ltd.
Burroughs Wellcome and Co.
Edwin Müller KG
Globe News Service Ltd.
National Pharmaceutical Union
Imperial Chemical Industries Ltd.
Ortho Pharmaceutical Ltd.
Olympia Ltd.

Consultants acquired

Roger Williams Technical and Economic Services Inc., a chemical market research organisation, has acquired the consulting firm of George Lewi and Partners, London. Mr. T. D. O'Keeffe, executive partner of the Lewi organisation, has been appointed vice-president and European manager of the Williams corporation. The London office will be at 7 Hanover Square, Hanover Court, W.1.

THE CHEMICAL MARKET

CHEAPER SOLVENTS

LONDON.—There are several changes in our list compared with the previous one (October). The most notable reductions have been in solvents—**ethyl acetate** and **alcohol** and **butyl alcohol** are appreciably cheaper. **Formaldehyde** has also come down, so has **dimethyl sulphate, aluminium stearate** and **citric acid.** One cwt. lots of **Aspirin** are cheaper. Among the important increases are **borax** and **boric acid, nitric acid, soda ash, magnesium chloride** and **zinc oxide.** There are the usual fluctuations in gums and waxes.

FINE CHEMICALS

Acetanilide 12½ kg. 7s. 4d. kg.
Arsenious oxide B.P.
7-lb. lots 1s. 9d. lb.
1-cwt. lots 1s. 2d. lb.
Ascorbic acid
100 kg. £4 14s. kg.
Aspirin
56 lb. 5s. 2d. lb.
1-cwt. 4s. 8d. ,,
5-cwt. lots 4s. 10d. ,,
Atropine
Sulphate, 500 g. £59 18s. 6d. kg.
Alkaloid, 500 g. £68 15s. kg.
Benzene B.P.C. 28-lb. lots 1s. 8d. lb.
Benzoic acid 12½ kg. 7s. 4d. kg.
Benzyl benzoate
According to pack 5s. to 7s. 2d. lb.
Bismuth oxide B.P.C. 1934
28-lb. lots 26s. 10d. lb.
Bismuth salts 28-lb. lots:
Carbonate 22s. 3d. lb.
Subgallate 21s. 1d. ,,
Salicylate 21s. 9d. ,,
Subnitrate 20s. 5d. ,,
Borax B.P.
Powder £60 10s. ton
Extra fine £61 10s. ,,
Boric acid B.P.
Crystal £99 ,,
Powder £96 10s. ,,
Bromine B.P.C. 7-lb. lots 6s. lb.
Caffeine 50 kg. 42s. 6d. kg.
Calamine 50 kg. 4s. kg.
Calcium gluconate
1 cwt. lots dlvd. 3s. 7d. lb.
Calcium glycerophosphate
50 kg. 28s. 6d. kg.
Calcium lactate B.P.
7-lb. lots 2s. 11d. lb.
1-cwt. lots 2s. 4d. ,,
Chloral hydrate 50 kg. 10s. kg.
Citric acid, B.P. Powder or granulated:
1-cwt. lots 198s. cwt.
5-cwt. lots 193s. ,,
Codeine
Alkaloid 100 g. £138 10s. kg.
Phosphate 100 g. £110 ,,
Cream of tartar
1-cwt. lots £12 5s. cwt.
5-cwt. lots £12 3s. ,,
Ephedrine
Hydrochloride 3 kg. £7 1s. 1d. kg.
Alkaloid 3 kg. £12 7s. ,,
Sulphate 3 kg. £7 1s. 1d. ,,
Eucalyptol
1-cwt. lots 11s. lb.
5-cwt. lots 10s. 6d. ,,
Ferri ammonium citrate B.P.
1-cwt. lots, scales 4s. 5½d. lb.
1-cwt. lots, granules 3s. 7½d. ,,
Ferrous gluconate
1-cwt. lots dlvd. 6s. 3d. lb.
Gallic acid B.P.C.
1-cwt. lots 10s. ,,
Gluconic acid technical 50%
Minimum 12-gal. drums
19s. gal., drums extra, returnable
Glucono delta lactone
1-ton lots dlvd. 5s. net lb.
Glycerophosphoric acid
24 litres 11s. 10d. litre
Glycine (amino acetic acid)
12½ kg. 18s. 10d. kg.
Hexyl resorcinol 10 kg. £7 10s. ,,
Hydroquinone 12½ kg. 23s. 10d. ,,
Iodides
Ethyl 4 kg. bottles 62s. 9d. kg.
Mercury, red B.P.C.
12½ kg. lots 61s. 3d. ,,
Potassium B.P.
12½ kg. lots 15s. 5d. ,,
Sodium B.P.
12½ kg. lots 22s. ,,
Iodine, Chilean crude,
99% min. in wooden casks 15s. kg.
Iodoform
12½ kg. and under 50 kg. 42s. 6d. kg.
Lactose 50 kg. 3s. 2d. kg.
Lithium salts 5-cwt. lots
Benzoate 10s. lb.
Carbonate B.P.C. 11s. 3d. ,,
Chloride (commercial) powder
11s. ,,
,, granular 10s. 9d. ,,
Hydroxide 9s. 9d. ,,
Citrate B.P.C. 9s. ,,
Sulphate 8s. 6d. ,,
Salicylate, 10 cwt., dlvd. 9s. 9d. ,,
Magnesium carbonate B.P.
Light cwt. lots dlvd. £129 ton
Magnesium trisilicate 28-lb. packs
28-lb. lots 4s. 3d. lb.
1-cwt. lots 3s. 10d. ,,
5-cwt. lots 3s. 7d. ,,
Bulk rates for larger quantities are from 3s. 1d. lb. in 1-ton lots
Manganese hypophosphite B.P.C.
7-lb. lots 13s. 11d. lb.
1-cwt. lots 12s. 11d. ,,
Mercuric chloride B.P.
50-kg. lump 48s. 6d. kg.
Methyl salicylate 1-cwt. lots 3s. 3d. lb.
Morphine
Alkaloid, 100 g. £138 18s. 4d. kg.
Nicotinamide 1 kg. £2 16s. 6d. kg.
Nicotinic acid
12½ kg. 33s. 9d. kg.
1 kg. 36s. ,,
Oleine, B.P. extra pale, 3/4 cwt. drums returnable carriage paid G.B.
£160 ton
Phenolphthalein 50 kg. 24s. 3d. kg.
Phosphoric acid B.P.
(s.g. 1·750) 10-carboy lots 1s. 4d. lb.
Potassium permanganate B.P.
1-cwt. lots dlvd. 1s. 11½d. lb.
Procaine hydrochloride (foreign)
2 kg. 59s. kg.
Quinine 1-oz. lots 4s. 4d. oz.
Riboflavin
100 g. 5½d. g.
10 g. 7d. ,,
Saccharin
500 g. £7 4s. for this quantity
Salicylic acid
B.P., dlvd. 3s. 2½d. to 5s. 6d. lb.
Silver nitrate
500 g. 5s. 2$^{5}_{16}$d. oz.
Sodium benzoate B.P.
1 cwt. lots 2s. 9½d. lb.
1-ton lots 2s. 7½d. ,,
Sodium gluconate technical
3-cwt. lots dlvd. 3s. net lb.
Sodium salicylate
50 kg. 8s. 8d. kg.
12½ kg. 9s. ,,
Sodium thiosulphate
Crystals, photographic quality
1-ton lots 49s. cwt.
Stearic acid B.P.C. flake, carriage paid G.B. £154 ton
Strychnine 25 oz.
Alkaloid 8s. oz.
Hydrochloride 8s. ,,
Sulphate 7s. ,,
Sulphaguanidine
12½ kg. 33s. kg.
50 kg. 32s. ,,
Sulphanilamide
12½ kg. 16s. 6d. kg.
50 kg. 15s. 4d. ,,
Sulphathiazole 12½ kg. 39s. 9d. ,,
Tannic acid B.P. Levis
1-cwt. lots 10s. lb.
Tartaric acid, B.P.
Powder or granulated,
10 cwt. or more £15 cwt.
Terpineol B.P.
40-gal. drums 2s. 4½d. lb.
1-cwt. lots 2s. 7d. ,,
Theophylline B.P.
500 g. 27s. 6d. for this quantity
Thiamine hydrochloride
100 g. 4d. g.
1 kg. £11 15s. kg.
Thioglycollate
Ammonium 12s. 4d. to 16s. 4d. lb.
Calcium:
7-lb. lots 17s. 3d. ,,
5-cwt. lots 14s. 3d. ,,
α-Tocopherol 25-g. lots 11d. g.
Vanillin 23s. 6d. to 30s. 6d. lb.
Zinc oxide B.P.
2-ton lots £122 10s. ton

GENERAL CHEMICALS

Acetic acid 1-ton lots dlvd.
80% Technical £99 ton
80% Pure £105 ,,
Glacial B.P. £114 ,,
99-100% Glacial £111 ,,
98-100% Glacial £108 ,,

Acetic anhydride
1-ton lots dlvd. £128 ton
Acetone
5-gal. drums, free, non-returnable £128 ton
40 to 45-gal. drums, 10-ton lots £88 ,,
Alum, potassium granular crystals
50 kg. 1s. 2d. kg.
Aluminium hydroxide B.P.C. 34
28-lb. lots 2s. 4d. lb.
Aluminium stearate
(Precipitate) 1-ton lots £253 10s. ton
Ammonia
Persulphate £6 13s. 6d. cwt.
Phosphate: Mono- £106 ton
Di- £97 10s. ,,
Amyl acetate
B.S.S. 10 tons and over £251 ton
Technical £249 ,,
Amyl alcohol
Technical in 1-ton lots £256 ton
Arsenic White powdered ex store £42 ton
n-Butyl acetate
10-ton lots £173 ton
n-Butyl alcohol
10-ton lots £132 ton
Calcium chloride
Solid 70 to 72%, 8-ton lots dlvd. £16 10s. ton
Calcium oxide (Lime)
Ex marble 28-lb. lots 3s. 10d. lb.
Caustic soda
Solid 1-ton lots, from £37 16s. 6d. ton
Chloroform B.P. ½-ton lots 2s. 11½d. lb.
Chromic acid
Dlvd. U.K. (less 2½%) 2s. 0¼d. to 2s. 0¾d. lb.
DDT 3s. 0½d. to 3s. 2d. lb.
2 : 4-Dichlorophenoxyacetic acid
99% pure, 1-cwt. bags £320 ton
Dimethyl sulphate 440 lb. drum lots 1s. 8d. lb.
Ether (Diethyl ether)
Tech. B.S.S. and Solvent B.P.
1-ton lots in drums 2s. lb.
Ethyl acetate 10-ton lots £131 ton
Ethyl alcohol
95% Gay Lussac 66·0 o.p.
over 300,000 proof gallons per year in tank wagons
3s. 10¼d. per proof gal.
Ferrous sulphate 50 kg. 1s. 4d. kg.
Formaldehyde
40% by volume dlvd. England
1-ton lots £37 15s. ton
Glycerin
1·2627 s.g. chem. pure, 5 tons and up, 5-cwt. drums £241 10s. ton
1·2627 s.g. technical grade, 5 tons and up, 5-cwt. drums £236 10s. ton
Hexamine
1-ton lots
Technical, bulk 1s. 7¼d. lb.
B.P.C. 1s. 10¼d. lb.
Hydrochloric acid
Commercial 18s. 6d. cwt.
Hydrogen peroxide
27·5% weight £119 ton
35% weight £143 ,,
Lactic acid (1-ton lots)
Pale tech. 44% by weight 1s. 3¼d. lb.
Dark tech. 44% by weight 9¼d. lb.
Magnesium chloride
Solid (ex wharf): 1-ton lots £18 10s. ton
Magnesium sulphate £15 ton
Mercurous chloride (calomel)
50 kg. 65s. kg.
Mercury sulphide, red
Ton lots and over 30s. 6d. lb.
Methylated spirits (Industrial)
Perfumery quality 500 gal. and upwards: gal.
61 o.p. 7s. 2½d.
74 o.p. 7s. 10d.
5 to 10 gal.:
61 o.p. 8s. 8d.
74 o.p. 9s. 3½d.
Methyl ethyl ketone
10 tons dlvd. in drums £143 ton
Methyl isobutyl carbinol
10 tons and up, in drums, dlvd. £163 ton
Methyl isobutyl ketone
10 to 50 tons, in drums, dlvd. £169 ton
Naphthalene
Crystal, dlvd., 4-ton lots, spot £66 ton
Ball and flake (ditto) £86 15s. ,,
Nickel sulphate
dlvd. ton lots £170 ton
Nitric acid 70% intermediate £36 ton
Pentachlorphenol
Flake, technical, 1-ton lots, dlvd. 2s. 2d. lb.
Phenol Crystals:
Under 1 ton dlvd. from 1s. 7d. lb.
10 tons and over dlvd. in returnable drums from 1s. 4½d. lb.
Phthalates
10-ton lots in drums
Diethyl (B.S.) £193 10s. ton
Dimethyl (B.S.) £185 ton
Potassium bromide
50 kg. 5s. 6d. kg.
12½ kg. 5s. 8d. ,,
Potassium carbonate
Calcined 96 to 98% (1-ton lots ex store) £75 10s. ton
Hydrated (1-ton lots) £74 10s. ,,
Potassium fluoride
28-lb. lots 5s. 1d. lb.
Potassium sodium tartrate
5-cwt. lots £10 cwt.
Soda ash
1-ton lots dlvd., from £19 16s. 6d.
Sodium cyanide
96-98% £130 ton
Sodium hydroxide 28-lb. lots:
sticks (1-lb. bottles) 4s. 3d. lb.
pellets ,, ,, 3s. 9d. ,,
Sodium metal 28 lb. lots 3s. 8d. ,,
Sodium metasilicate
Dlvd. U.K. in ton lots £26 ton
Sodium phosphate
Dlvd. ton lots: Di-sodium, crystalline £40 10s. ton
Anhydrous £88 ,,
Tri-sodium, crystalline £39 ,,
Anhydrous £86 ,,
Sodium silicate
according to quantity, grade and delivery point
8-ton lots £13 10s. ton
1-ton lots £17 ,,
Sodium sulphate Ex works:
(Glauber salt) £13 ton
(Salt cake) unground, full truck loads £8 16s. 6d. ton
Sodium sulphide
Broken, returnable drums, dlvd. ton lots £37 2s. 6d. ton
Flake, ditto £38 12s. 6d. ,,
Solid ditto £36 2s. 6d. ,,
Sodium sulphite
Commercial crystals 4-ton lots £28 10s. ,,
(Dlvd. London in 1-cwt. single non-returnable bags)
Sodium tripolyphosphate
1-ton lots £95 ton
Stannic chloride 28-lb. lots 8s. 11d. lb.
Stannous chloride 28-lb. lots 9s. 5d. lb.
Strontium carbonate
96-98% 28-lb. lots 3s. lb.
Sulphuric acid, ex-works, according to quality and quantity
B.O.V. 78% from 8s. to 10s. cwt.
C.O.V. 96% from 11s. to 14s. cwt.
Zinc chloride
28-lb. lots sticks 6s. 9d. lb.

OILS AND FATS

Palm kernel oil
Refined, deodorised, 2-ton lots, naked, ex-works £159 ton
Palm oil
Refined, deodorised, 2-ton lots, naked, ex-works £103 ton
Stearine
dlvd. free bags
Pristerene 64 flake £148 ton
Pristerene 62 flake £133 ,,
Pristerene 61 flake £113 ,,
A premium of £2 ton is charged for powder and £4 for block

GUMS AND WAXES

Agar Agar No. 1
Kobe strip 15s. lb.
Powder £1 ,,
Beeswax
Dar-es-Salaam spot (nominal) £26 cwt.
Sudan spot (duty paid) £24 5s. ,,
Bleached white (slab) £29 10s. ,,
Refined yellow (slab) £26 10s. ,,
Benzoin
Sumatra spot £26 10s. cwt.
Siam spot £2 7s. 6d. lb.
Candelilla Spot £23 cwt.
Carnauba
Prime, Spot £48 cwt.
Fatty grey £31 10s. ,,
Gum arabic Lump £9 15s. cwt.
Karaya Powder, Spot 3s. 8d. lb.
Paraffin wax
1-ton lots, acc. to grade £105 to £130 ton
Peru balsam 13s. 6d. lb.
Shellac
No. 1 orange £13 10s. cwt.
No. 2 orange £12 ,,
Transparent white 4s. 3d. lb.
Pale dewaxed 6s. ,,
Tragacanth
No. 1 spot £134 cwt.
No. 2 spot £122 ,,
Pale leaf £51 ,,
Amber £38 ,,
Brown to Red £27 ,,

NEW TRADE MARKS

APPLICATIONS

Pharmaceuticals

TENULES.—792,611. *Boots Pure Drug Co. Ltd.*

PRO-ACTIDIL. — 792,623. *Wellcome Foundation Ltd.*

SUPRACILLIN.—792,963. *Beecham Research Laboratories Ltd.*

HEPROVAX.—793,081. *Willows Francis Ltd.*

VERSITOL.—792,554. *Bell and Sons Ltd.*

SECRODYL.—792,278. *British Drug Houses Ltd.*

MYCINGAN.—792,705. *C. H. Boehringer Sohn.*

ASPRO.—756,429. *Aspro-Nicholas Ltd.*

EUROSPITAL.—784,745. *Importex Chimici Farmaceutici.*

MELPREX.—785,787. *American Cyanamid Co.*

KOLBAN.—786,121. *Mentholatum Co. Ltd.*

BIT-ABS.—786,938. *Norma Chemicals Ltd.*

DUROPHET.—787,278. *Riker Laboratories Ltd.*

ELPIRON.—788,108; COLSAN.—788,109. *Imperial Chemical Industries Ltd.*

FEBS.—788,177. *Boots Pure Drug Co. Ltd.*

RIKOSOL.—789,784. *Riker Laboratories Ltd.*

BEKAMIN.—789,743; EPIVAX-X.—791,170; NEO-EPIVAX.—791,172. *Wellcome Foundation Ltd.*

HYCODORM.—791,339. *Duncan Flockhart and Co. Ltd.*

PALEROL.—791,404. *Sandoz Products Ltd.*

RESOTREN.—791,552. *Farbenfabriken Bayer A.G.*

GATRACIL.—791,560. *Cilag A.G.*

VETAPTINE.—792,355. *A.B. Astra, Apotekarnes Kemiska Fabriken.*

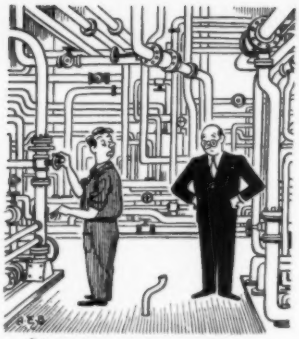
STELBID.—792,576. *Smith Kline and French Laboratories.*

EPIVAX-PLUS.—792,622. *Wellcome Foundation Ltd.*

DARITRAX.—792,762. *Chas. Pfizer and Co. Inc.*

DELOVAX.—792,887. *Wellcome Research Laboratories.*

INFONUTROL.—793,003. *A.B. Astra, Apotekarnes Kemiska Fabriken.*



"I'VE OFTEN WONDERED MYSELF"

Cosmetics and toilet preparations

RANI.—784,879. *Indola N.V.*

TINTELLE.—788,263. *Golden Ltd.*

NUTROL.—B788,582. *Boots Pure Drug Co. Ltd.*

NEVSIL.—789,946. *Peel and Campden Ltd.*

BRETALIN. — 790,809. *Prince Regent Tar Co. Ltd.*

VELVETTES.—790,986. *Morny Ltd.*

ALBATRICE.—791,105. *P. N. Belfield.*

PAMPER.—792,627. *County Laboratories Ltd.*

COLORETE.—793,041. *Eau de Cologne & Parfümerie-Fabrik.*

DESYNOVA.—793,953. *Röhm & Haas G.m.b.H.*

POLINET.—788,812. *G. W. Scaddan and Co. Ltd.*

FANTABULOUS. — 793,737. *Maurice Norton.*

PREV.—789,379. *Orchard Paper Co.*

PINK CLOUD.—778,449. *Beauty Counselors of London Ltd.*

TINTOREL.—788,262. *Golden Ltd.*

WONDRA.—B792,519. *Thomas Hedley and Co. Ltd.*

REGENCY GROOM.—792,651. *Gorney Ltd.*

NULON.—793,507. *Reckitt and Sons Ltd.*

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NEW PATENTS

COMPLETE SPECIFICATIONS ACCEPTED

Pharmaceuticals

Aroxyaliphatic compounds. *May and Baker Ltd.* 827,372.

Manufacture of tablets. *MacLeans Ltd.* 827,529.

Sulphonamides. *Merck and Co. Inc.* 826,924.

Agent for treating glycosuria. *K. R. Binning.* 827,139.

Hydroquinone compounds and process for their manufacture. *Ciba Ltd.* 826,917.

Method of preparing ribosides of nucleic acid bases. *Spofa, Spojene Farmaceuticke Zavody, Narodni Podnik.* 827,441.

Pyrimidine derivatives. *Ortho Pharmaceutical Corporation.* 827,530.

Materials having vitamin E activity. *Vitamins Ltd.* 827,391.

Pyridazone compounds and process for their manufacture. *Ciba Ltd.* 826,640.

1- phenyl - 3 - halogeno - 5 - piperazinopyridazine - (6) compounds, and a process for their manufacture. *Ciba Ltd.* (Divided out of 826,440.)

Hypoglycæmic sulphonamide derivatives. *Astra Apotekarnes Kemiska Fabriker A.B.* 826,539.

Naphthoquinone derivatives. *Farbenfabriken Bayer A.G.* 826,533.

6 - methoxy - 8 - (5 - *n* - propylaminopentylamino) quinoline and acid addition salts thereof. *Sterling Drug Inc.* 826,811.

4 - carbalkoxy - 4 - phenyl piperidine derivatives and processes for preparing them. *Laboratoria Pharmaceutica Dr. C. Janssen N.V.*, and *Nederlansche Combinatie Voor Chemische Industrie N.V.* 826,803.

Therapeutic compositions. *C. Pfizer and Co. Inc.* 826,676.

1 : 3 : 5-triazine compound and process for its manufacture. *Ciba Ltd.* 825,072.

Triazine derivatives. *May and Baker Ltd.* 824,908.

Quinone compounds and process for their manufacture. *Ciba Ltd.* 825,557.

Retrocortin derivatives. *Merck and Co. Inc.* 826,367; 826,368.

1 - thienyl - 3 - amino - propanol derivatives. *Sterling Drug Inc.* 826,487.

Substituted piperazines and methods for obtaining same. *Parke, Davis and Co.* 826,496.

Steroids

Process for the manufacture of polyoxygenated dehydro-steroids. *Ciba Ltd.* 827,182.

Steroid esters and their preparation. *Ciba Ltd.* 826,953.

Steroids and the manufacture thereof. *Upjohn Co.* 826,630.

Steroids and the manufacture thereof. *Upjohn Co.* 826,629.

Pest control chemicals

Compositions for treating nematodes. *Spencer Chemical Co.* 826,532.

Alpha - (halophenoxy) - propionic acids and herbicidal compositions thereof. *Boots Pure Drug Co. Ltd.* 826,995.

Antibiotics

Antibiotics. *Laboratories Français de Chimiotherapie.* 826,756.

Purification of factor Z derivable from antibiotics E 129. *Glaxo Laboratories Ltd.* 826,704.